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Irradiation in the Production, Processing, and Handling of Food; Final Rule; Denial of Request for Hearing and Response to Objection

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

21 CFR Part 179

[Docket Nos. 81N-0004 and 84F-0230]

Irradiation in the Production, Processing, and Handling of Food

AGENCY: Food and Drug Administration.

ACTION: Final rule; denial of requests for hearing and response to objections.

SUMMARY: The Food and Drug Administration (FDA) is denying the requests that it has received for a hearing on the final rules that amended the food additive regulations to authorize the use of gamma radiation for the treatment of pork to control *Trichinella spiralis* and for the treatment of certain other foods. After reviewing the objections to the two final rules and the requests for a hearing, FDA has concluded that none of the objections has provided the information necessary to justify a hearing. FDA, however, is amending the language in the regulation that describes minor dry ingredients that may be radiation sterilized because objections and experience have shown that this language is ambiguous.

DATES: The amendment in 179.26(b) (21 CFR 179.26(b)) is effective December 30, 1988; written objections on the amendment and requests for a hearing on the amendment by January 30, 1989.

ADDRESS: Written objections on the amendment to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Clyde A. Takeguchi, Center for Food Safety and Applied Nutrition (HFF-330), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-472-5740.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of July 22, 1985 (50 FR 29658), in response to a petition by Radiation Technology, Inc., FDA issued a final rule authorizing the irradiation of fresh pork to control *Trichinella spiralis*. FDA based its decision on data in the petition and in its files. The agency had published a notice announcing the filing of the petition (FAP 4M3789) in the **Federal Register** of July 23, 1984 (49 FR 29682).

In the **Federal Register** of April 18, 1986 (51 FR 13376), FDA issued a final rule, referred to herein as the "omnibus rule," that: (1) permitted manufacturers to use radiation at doses not to exceed 1 kilogray (kGy)(100 krad) to inhibit the growth and maturation of fresh foods and to disinfest food of arthropod pests; (2) permitted manufacturers to use radiation at doses not to exceed 30 kGy (3 Mrad) to disinfect dry or dehydrated aromatic vegetable substances (such as spices and herbs) of microorganisms; (3) required that foods that are irradiated be labeled to show this fact both at the wholesale and at the retail level; and (4) required that manufacturers maintain process records of irradiation for a specified period and make such records available for FDA inspection. FDA initiated this action by publishing a proposal in the **Federal Register** of February 14, 1984 (49 FR 5713).

A. Requests for hearing on final rules

Section 409(f) of the Federal Food, Drug, and Cosmetic Act (the act), 21 U.S.C. 348(f), provides that, within 30 days after publication of an order relating to a food additive regulation, any person adversely affected by such an order may file objections specifying with particularity the provisions of the order considered objectionable, stating reasonable grounds for the objections, and requesting a public hearing on such objections.

Under 21 CFR 171.110 of the food additive regulations, objections and requests for a hearing are governed by 21 CFR Part 12 of FDA's regulations. Under 21 CFR 12.22(a), (1) each objection must be submitted on or before the 30th day after the date of publication of the final rule; (2) each objection must be separately numbered; (3) each objection must specify with particularity the provision of the regulation or proposed order objected to; (4) each objection on which a hearing is requested must specifically so state; failure to request a hearing on an objection constitutes a waiver of the right to a hearing on that objection; and (5) each objection requesting a hearing must include a detailed description and analysis of the factual information to be presented in support of the objection. Failure to include a description and analysis for an objection constitutes a waiver of the right to a hearing on that objection.

FDA received 59 objections to the irradiated pork rule and 245 objections to the omnibus rule. Many of the objections expressed general opposition to food irradiation but identified no substantive question to which the agency can respond. Because these objections failed to raise any basis on which to question the validity of the final rules, the agency is denying them.

Seventeen objections to the irradiated pork rule and 53 objections to the omnibus rule pointed to a specific aspect of the rule but did not request a hearing. Twenty objections to the irradiated pork rule and 12 objections to the omnibus rule requested a hearing. These objections are addressed below.

Some of the objections requested a stay of the regulations. In the **Federal Register** of February 23, 1987 (52 FR 5450), FDA denied these requests because the public interest did not require a stay. FDA evaluated each of the contentions made in support of a stay and concluded that they failed to create significant doubts about the safety of the food irradiated under the conditions of either of the two regulations.

B. Standard for granting a hearing

The criteria for deciding whether to grant or deny a hearing are stated in 21 CFR 12.24(b). The regulation states that a hearing will be granted when the material submitted shows the following:

(1) There is a genuine and substantial issue of fact for resolution at a hearing. A hearing will not be granted on issues of policy or law.

(2) The factual issue can be resolved by available and specifically identified reliable evidence. A hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions.

(3) The data and information submitted, if established at a hearing, would be adequate to justify resolution of the factual issue in the way sought by the person. A hearing will be denied if the Commissioner concludes that the data and information submitted are insufficient to justify the factual determination urged, even if accurate.

(4) Resolution of the factual issue in the way sought by the person is adequate to justify the action requested. A hearing will not be granted on factual issues that are not determinative with respect to the action requested, e.g., if the Commissioner concludes that the action would be the same even if the factual issue were resolved in the way sought, or if a request is made that a final regulation include a provision not reasonably encompassed by the proposal.

(5) The action requested is not inconsistent with any provision in the act or any regulation in this chapter particularizing statutory standards. The proper procedure in those circumstances is for the person requesting the hearing to petition for an amendment or waiver of the regulation involved.

(6) The requirements in other applicable regulations, e.g., 21 CFR 10.20, 12.21, 12.22, 314.200, 430.20(b), 514.200, and 601.7(a), and in the notice promulgating the final regulation or the notice of opportunity for hearing are met.

A party seeking a hearing is required to meet a "threshold burden of tendering evidence suggesting the need for a hearing." *Costle* v. *Pacific Legal Foundation,* 445 U.S. 198, 214–215 (1980), *reh. den.,* 445 U.S. 947 (1980), citing *Weinberger* v. *Hynson, Westcott & Dunning, Inc.,* 412 U.S. 609, 620–621 (1973). An allegation that a hearing is necessary to "sharpen the issues" or to "fully develop the facts" does not meet this test. *Georgia Pacific Corp.* v. *U.S. E.P.A.,* 671 F.2d 1235, 1241 (9th Cir. 1982). If a hearing request fails to identify any evidence that would be the subject of a hearing, there is no point in holding one.

A hearing request must not only contain evidence, but that evidence must raise a material issue of fact concerning which a meaningful hearing might be held. *Pineapple Growers Ass'n* v. *FDA,* 673 F.2d 1083, 1085 (9th Cir. 1982). Where the issues raised in the objection are, even if true, legally insufficient to alter the decision, the agency need not grant a hearing. *Dyestuffs and Chemicals, Inc.* v. *Flemming,* 271 F.2d 281 (8th Cir. 1959), *cert. denied,* 362 U.S. 911 (1960). FDA need not grant a hearing in each case where an objector submits additional information or posits a novel interpretation of existing information. (See *United States* v. *Consolidated Mines & Smelting Co.,* 455 F.2d 432 (9th Cir. 1971)). Stated another way, a hearing is justified only if the objections are made in good faith, and if they "draw in question in a material way the underpinnings of the regulation at issue." *Pactra Industries* v. *CPSC,* 555 F.2d 677 (9th Cir. 1977). Finally, courts have uniformly recognized that a hearing need not be held to resolve questions of law or policy. (See *Citizens for Allegan County, Inc.* v. *FPC,* 414 F.2d 1125 (D.C. Cir. 1969); *Sun Oil Co.* v. *FPC,* 256 F.2d 233, 240 (5th Cir.), *cert. denied,* 358 U.S. 872 (1958)).

Even if the objections raise material issues of fact, FDA need not grant a hearing if those same issues were adequately raised and considered in an earlier proceeding. Once an issue has been so raised and considered, a party is estopped from raising that same issue in a later proceeding without new evidence. The various judicial doctrines dealing with finality are validly applied to the administrative process. In explaining why these principles "self-evidently" ought to apply to an agency proceeding, the D.C. Circuit wrote:

> The underlying concept is as simple as this: Justice requires that a party have a fair chance to present his position. But overall interests of administration do not require or generally contemplate that he will be given more than a fair opportunity.

Retail Clerks Union, Local 1401, R.C.I.A. v. *NLRB,* 463 F.2d 316, 322 (D.C. Cir. 1972). (See *Costle* v. *Pacific Legal Foundation, supra* at 1106. See also *Pacific Seafarers, Inc.* v. *Pacific Far East Line, Inc.,* 404 F.2d 804 (D.C. Cir. 1966)).

C. Objections to the pork regulation and the omnibus regulation

Six of the 20 objections to the irradiated pork rule that requested a hearing did not point to any specific aspect of the rule. Six of the 12 objections to the omnibus rule that requested a hearing were either form letters or objections that requested a hearing on the subject but that did not point to any specific aspect of the rule that they sought to challenge. Because no evidence was submitted in support of these objections, they raise no factual issue for resolution and, therefore, do not justify a hearing. The agency will not discuss them further.

One objection to the omnibus rule requested a hearing but was not submitted to FDA until after the close of the objection period. Hence, this objection failed to satisfy the requirements of 21 U.S.C. 348(f)(1) and need not be considered further by the agency. *ICMAD* v. *HEW,* 574 F.2d 553, 558 n.8 (D.C. Cir.), *cert. denied,* 439 U.S. 893 (1978). Issues raised in the tardy objection were also raised in other objections, however, and thus will be addressed in this document.

One of the objectors to the omnibus rule, the Health and Energy Institute, on behalf of itself and the Environmental Policy Institute (HEI), submitted numerous objections. However, HEI submitted very little evidence in support of these objections. HEI did promise, with respect to several of its objections, to submit evidence at any hearing that is held. FDA evaluated these objections. Most did not present enough information to draw the agency's action into question in a material way. These the agency proceeded to consider without further information from HEI. However, some of the objections did suggest the possible existence of a substantial issue of fact but did not identify enough evidence to determine whether these objections provided an appropriate basis for an evidentiary hearing. On February 2, 1987, the agency wrote to HEI and asked it to submit additional information on this latter group of objections to aid FDA in deciding whether any of them justified a hearing (Ref. 1). HEI provided additional information on March 6, 1987 (Ref. 2).

On May 5, 1987, the agency again wrote to HEI and requested two references that HEI had cited in its March 6, 1987, submission but that were not available in FDA's files (Ref. 3). FDA gave HEI 14 days to supply copies of these references. On May 21, 1987, HEI provided one of these references, an article cited by that reference, and two additional articles, but it was unable to obtain the second reference that FDA had requested (Ref. 4).

There was considerable overlap in the objections to the two rules on irradiation. Some objections raised in response to the pork rule are, in fact, more applicable to the omnibus rule. Therefore, FDA will deal with the objections to both rules together.

Because HEI provided the most detailed objections, its objections will be the focus of much of this document. Where other objections raised the same or a similar issue as one raised by HEI, FDA will incorporate these other objections in its description of the issue. The agency has grouped together all objections that raise the same concern and has analyzed most of the objections according to the following four-part format: (1) A statement of a specific position or conclusion set forth by FDA in the final rule; (2) a summary of the challenge to that conclusion and of the basis for the request for a hearing, if one was made; (3) a discussion of whether the objection justified a hearing on that objection; and (4) where appropriate, a review of the evidence relevant to the objection.

II. Safety of Food Irradiation

In both the pork and omnibus final rules, FDA concluded that food irradiated under specified conditions is safe. FDA based its conclusion primarily on an analysis (49 FR 29682; 51 FR 13376 at 13378) that demonstrated that foods irradiated at doses permitted under these final rules undergo only minimal chemical change and are toxicologically indistinguishable from nonirradiated foods. The agency considered the sensitivity of a variety of state-of-the-art toxicology testing regimens, including extraction and concentration of radiolytic products, to determine the best way of evaluating the safety of irradiated foods (Ref. 5). The agency's analysis also included a review by the Bureau of Foods Irradiated Foods Task Group (Task Group) of all available

animal feeding studies with irradiated foods (Ref. 6). The Task Group concluded that the studies did not provide evidence that irradiated food caused adverse toxicological effects (51 FR 13376 at 13378). Based on these reviews and on the information in the agency's files, the agency concluded that there is an adequate margin of safety for foods irradiated under the conditions of these final rules, and that no further toxicological testing need be required (51 FR 13376 at 13378.)

Several objections stated that FDA's conclusion on the safety of irradiation is based on assumptions and theoretical analyses. These objections stated that the agency should have relied on evidence such as animal feeding studies. The most detailed statement of this point was made by HEI in its objection to the omnibus rule. HEI stated that: "* * * the FDA promulgated a regulation to allow increased food irradiation, declaring the process and resulting food safe, based on mere assumptions of safety, rather than on scientific tests which demonstrate the safety of the process, and the FDA has ignored scientific testing data and other scientific evidence which suggests adverse impacts from consuming irradiated food * * *." In support of this general statement, HEI made 22 specific objections, each of which, it claimed, justified a hearing. The agency has considered each of these objections, and it finds that none of them presents a genuine and material issue of fact that would justify a hearing on the general issue that HEI has raised.

A discussion of the objections related to the safety of food irradiation follows.

A. Estimates of consumption of irradiated foods

In 1979, FDA established the Bureau of Foods Irradiated Food Committee (BFIFC) to review the existing agency policy concerning the irradiation of foods (Ref. 5). BFIFC was charged to recommend "toxicologic [testing] requirements appropriate for assessing the safety of irradiated food * * *, where the degree of testing is consistent with the potential risk as predicated on the level of human exposure."

1. BFIFC exposure estimates

HEI stated that "BFIFC used incorrect dietary data to declare safety." In support of this objection, HEI stated that:

> BFIFC assumed that consumption of irradiated food would constitute only 10 percent of the human diet (51 FR 13377), despite petitions before the agency to allow irradiation of additional foods that might increase total consumption of foods that have been irradiated.

(Paragraph I.1. from HEI's May 19, 1986, objection.)

A hearing will not be granted on factual issues that are not determinative with respect to the action requested (21 CFR 12.24 (b)(4)). In this objection, HEI has challenged the correctness of BFIFC's conclusions on the grounds that BFIFC was incorrect on the portion of the diet that will be irradiated. However, the BFIFC report makes clear that its conclusions were not based on the portion of the diet that would be irradiated. In concluding that food irradiated at doses not exceeding 1 kGy (100 krad) is safe for human consumption, BFIFC stated: "This [conclusion] is based solely on an estimate of the concentration of individual URP's [unique radiolytic products] produced by the radiation dose to the food, and pertains even if a *high* portion of the total human diet is irradiated at 100 krad" (emphasis added) (Ref. 5). Therefore, because this objection fails to challenge the finding that provides the actual basis for BFIFC's conclusion, it does not provide the basis for a hearing.

Furthermore, HEI's objection that BFIFC assumed that consumption of irradiated food would constitute only 10 percent of the human diet is incorrect. What BFIFC said was that conceivably 40 percent of a person's diet could be irradiated if the process is widely adopted, but that it was unlikely that more than 10 percent would be irradiated (51 FR 13376 at 13377). BFIFC's considerations were not restricted to the foods permitted to be irradiated under this rule but included all foreseeable applications of food irradiation.

In reaching its own conclusion about the safety of irradiation, FDA did not rely solely on the BFIFC report, as HEI's objection seemed to imply. Instead, FDA relied on the totality of evidence before it, including the report from the Task Group and the other evidence referenced in the proposal and omnibus rule. On this basis, the agency concluded that irradiation of food under the conditions that it specified is safe.

2. Irradiation of Certain Aromatic Vegetable Substances

The agency decided that certain aromatic vegetable substances, such as dried spices and seasonings, can be irradiated safely at a dose of up to 30 kGy (3 Mrad) (51 FR 13376 at 13378). This decision was based primarily on two factors. First, FDA found that the amount of radiolytic products that would be consumed from irradiated spices and seasonings is so small that such irradiated foods can be considered safe (51 FR 13376 at 13380). Second, the agency determined that the aromatic vegetable substances allowed to be irradiated are not sources of nutrients (51 FR 13376 at 13381), and that nutrient losses that might result from irradiation of these ingredients are of no concern. Because of comments related to language on spice consumption in the BFIFC report, the agency noted in the omnibus rule that it had not based its safety decision on an assumption that total consumption of spices would not exceed 0.01 percent of the daily diet and, indeed, recognized that total consumption of all spices would exceed 0.01 percent (51 FR 13376 at 13380).

HEI in its objection, states that:

> The FDA contends that because foods such as *individual* spices comprise less than 0.01 percent of the total diet of an individual, consequences of eating such foods need not be addressed. This ignores the fact that the total amount of all spices will exceed 0.01 percent of the diet for a wide variety of persons, which under FDA's own regulation would require toxicological testing to be performed. However, the FDA then expands its food list for exposures up to 3 megarads to include other food items such as teas and seeds, which may constitute a far greater portion of an individual's diet, especially if that individual consumes several cups of tea a day or consumes seeds and nuts in large quantities. FDA totally fails to address the proportion of an individual[']s diet with regard to teas and seeds. Many vegetarians consume far more than 0.01 percent of their total diet in the form of teas or seeds such as sunflower seeds and alfalfa seeds. Evidence regarding dietary consumption of any foods that could be irradiated under the proposed new regulations would be presented at a public hearing.

(HEI Para. I.9.) (Emphasis by HEI.)

This objection does not provide any basis for a hearing. Whether spices constitute more than 0.01 percent of the diet is not an issue. The agency estimated in the omnibus rule, "a probable intake of dried spices and culinary herbs of up to 3 grams per person per day. For the general population, this constitutes 0.1 percent of the total diet of 3 kilograms." (51 FR 13376 at 13380.)

Nor has HEI justified a hearing on the safety of the consumption of irradiated spices at a level of 0.1 percent of the diet. In the omnibus rule, FDA concluded that consumption of irradiated spices at this level is safe (51 FR 13376 at 13380). In support of this conclusion, FDA relied upon the BFIFC report (Ref. 5), the Task Group report (Ref. 6), and on other information in its files. HEI has not tendered any evidence

that would challenge FDA's reliance on this material or that would suggest that this conclusion is not correct.

Moreover, HEI is not correct that under FDA's regulations, the fact that the amount of spices in the total diet will exceed 0.01 percent would require toxicological testing to be performed. FDA has not adopted regulations that require toxicological testing of a food ingredient if that ingredient constitutes a certain portion of the diet, and HEI has not cited any regulation that imposes such a requirement. HEI appears to be referring to a recommendation in the BFIFC report that was mentioned in the advance notice of proposed rulemaking (ANPR) (46 FR 18992; March 27, 1981). The BFIFC report took the position that irradiation of any individual ingredient that constituted less than 0.01 percent of the diet was not of sufficient concern to require further toxicological testing.

This report was a recommendation to the agency, not a regulation. In response to a comment on the proposal, the agency stated that radiolytic products from different spices are likely to be different, and that the intent of the recommendation in BFIFC's report was not to set a precise dietary percentage limit of 0.01 percent but rather to acknowledge that the amounts of radiolytic products that would potentially be consumed from irradiated dried spices and seasonings are so small that such irradiated foods can be considered safe as ordinarily used. Based on the BFIFC report and other information available to it, the agency concluded that irradiation of spices under the conditions permitted by the regulation is safe (51 FR 13376 at 13380). HEI has not provided any basis on which to contest this conclusion. Therefore, this objection does not provide any basis for a hearing.

Nonetheless, HEI has pointed to a possible source of confusion caused by the wording of the regulation. In final rules issued on July 5, 1983 (48 FR 30613 at 30614), and April 18, 1985 (50 FR 15415), the agency listed numerous spices, seasonings, and culinary herbs that are permitted to be irradiated. The list included several seeds, such as caraway seeds and celery seeds, as well as substances such as orange petals and chamomile used to prepare herbal teas. In the omnibus final rule, FDA decided to describe these substances generically rather than by a specific list. It adopted the term "aromatic vegetable substances." The agency established five categories of such substances that included all the individual substances on the original list, as well as other aromatic vegetable substances used as minor ingredients (51 FR 13376 at 13381).

This generic listing has been the source of some confusion. The agency has consistently referred to these dry or dehydrated aromatic vegetable substances that can be irradiated at doses not exceeding 30 kGy as ingredients that are not sources of nutrients but that are used in small amounts solely for their aromatic and flavoring characteristics. HEI has pointed to two examples of seeds—sunflower seeds and alfalfa seeds—that are not necessarily used in small amounts for their aromatic and flavoring characteristics but that may be used in other ways and that may actually be sources of nutrients. Grains (such as wheat, rice, or oats) are also examples of seeds that would not be considered "aromatic vegetable substances" within the meaning of this regulation. Only seeds that are used solely for their aromatic and flavoring properties, and that are not important sources of nutrients, are aromatic vegetable substances that may be irradiated under this regulation at doses not exceeding 30 kGy to control microorganisms. To make this clear, FDA is adding the phrase "when used as ingredients in small amounts solely for flavoring or aroma" after the term "aromatic vegetable substances" in § 179.26(b).

The agency has also found that the term "vegetable seasonings" has not been well understood. This term could be interpreted to include numerous substances whose irradiation at the 30 kGy level FDA did not intend to approve. For example, FDA intended this term to mean seasonings that are used in a manner similar to spices and never intended it to include vegetable pieces used for seasoning purposes under various standards of identity, such as 21 CFR 155.130 (Canned corn). Vegetable pieces used in such a manner may constitute a larger portion of the diet than the agency considered. To eliminate this confusion, the agency is revising the term "vegetable seasonings" to read "vegetable seasonings that are used to impart flavor but that are not either represented as, or appear to be, a vegetable that is eaten for its own sake." Thus, onion pieces could not be irradiated, while onion powder could be. The agency believes that all of the substances that it intended to permit to be irradiated will be adequately described by this new terminology.

In addition, because FDA approved the irradiation of specific substances used in herbal teas in the July 1983 and April 1985 final rules, the agency listed "teas" among the categories of dry aromatic vegetable substances in the omnibus rule. Herbal teas, however, are not the same as the product commonly known as "tea", i.e., the product derived from the shrub *Thea sinensis L.* The agency is unaware of any reason to irradiate tea itself, as opposed to those products called "herbal teas," and has no information that anyone has ever proposed to irradiate tea. The agency believes that it erred in including the word "teas" in the regulation because the term "culinary herbs" encompasses any dry herbal tea product.

Therefore, the agency is modifying the wording of paragraph § 179.26(b) as follows: (1) To add the phrase "when used as ingredients in small amounts solely for flavoring or aroma" after the term "aromatic vegetable substances"; (2) to add the words "that are used to impart flavor but that are not either represented as, or appear to be, a vegetable that is eaten for its own sake" after the words "vegetable seasonings"; and (3) to remove the word "teas" from the list of types of substances that may be irradiated at the 30 kGy level.

B. Need for Toxicological Testing

The agency concluded that foods irradiated at the levels permitted by the regulation need not be tested toxicologically because the types and concentrations of radiolytic products in these foods after irradiation would be such that even with the most sensitive toxicological testing it would not be possible to measure any toxicological effects (51 FR 13376 at 13378).

HEI stated:

> BFIFC admitted that "some radiolytic products may be unique to irradiated foods," termed such chemicals "unique radiolytic products (URP's)" and then *assumed* that such URP's would not constitute more than 3 parts per million concentration in food (51 FR 13377). Each food item could have its individual URP's, so a wide variety of URP's is possible in the fruits, vegetables, grains, and other foods that could be irradiated under the new regulation. The concentration of URP's is not the crucial factor, since cancer can be initiated by a single URP or carcinogenic chemical. FDA presents no scientific proof that those radiolytic products unique to irradiated foods are "chemically similar to known natural food components (and) are likely to be toxicologically similar also" (51 FR 13378). FDA should require extensive studies to be performed to demonstrate the safety of these chemicals before human consumption is permitted. Specifically, concentrated amounts [of] radiolytic products should be fed to animals in carefully controlled studies to test for potential mutagenicity and carcinogenicity, as suggested by Drs. Samuel Epstein and John Gofman in *Science* Vol. 223, p. 1354. Until these types of studies are performed there is

no basis for the wholesale approval of irradiation. Since FDA's regulation did not require studies to test for the long-term health impact of these chemicals, it is in violation of the Food, Drug and Cosmetic Act, and evidence will be presented at the public hearing.

(HEI Para. I.3.) (Emphasis by HEI.)

In this objection, HEI has made a number of allegations about the significance of FDA's decision not to require toxicological testing before concluding that irradiation of food in the circumstances set forth in § 179.26 is safe. However, HEI has failed to make an adequate proffer to support a hearing on any of these allegations.

Under FDA's regulations, a hearing will not be granted on the basis of mere allegations. (21 CFR 12.24(b)(2)). Consistent with this regulation, the relevant case law provides that where a party requesting a hearing only offers allegations without an adequate proffer to support them, the agency may properly disregard those allegations. *General Motors Corp.* v. *FERC,* 656 F.2d 791, 798 n. 20 (D.C. Cir. 1981). For example, FDA need not grant a hearing on HEI's claim that each irradiated food item has its own individual URP's because HEI has not presented any evidence to support this claim.

Furthermore, HEI's allegation that BFIFC *"assumed"* (emphasis by HEI) that "* * * URP's would not constitute more than 3 parts per million concentration in food * * * is also without support. As noted in the final rule, BFIFC based its estimate of the likely concentration of URP's in foods on a review of experimental data showing the amount and type of chemical change likely to be caused by a given amount of radiation (51 FR 13376 at 13377). HEI has not presented any evidence that challenges the basis for BFIFC's analysis or the agency's reliance on that analysis.

HEI asserts that the concentration of URP's is not the crucial factor but again has not provided any evidence or rationale to support its assertion. Even if HEI is correct that cancer can theoretically be initated by a single URP or carcinogenic chemical, to justify a hearing, HEI would have to provide some evidence that would reasonably link low levels of URP's to the causation of cancer. HEI has not presented any such evidence.

As discussed earlier in this document and in the omnibus rule, FDA examined all available data from animal feeding studies with irradiated foods and found no link between irradiated food and cancer (51 FR 13376 at 13378). Therefore, HEI's assertion is a mere allegation that is not supported by any evidence. FDA will not grant a hearing on the basis of such an assertion (21 CFR 12.24(b)(2)).

HEI's allegation that FDA has not presented scientific evidence that radiolytic products are chemically and toxicologically similar to known natural food components is untrue. The agency did cite specific articles on the radiation chemistry of food components in the proposed omnibus rule (49 FR 5714 at 5721, Ref. 7 to 12; see also 51 FR 13376 at 13380) and included other references in the administrative file (Docket No. 81N–0004). The agency considered this information in its safety evaluation of radiolytic products.

While FDA has the ultimate burden of proof when it approves the use of a food additive, in the sense that the agency must find the additive to have been shown safe, once the agency makes a finding in a listing document, the burden shifts to an objector to come forward with evidence that calls that finding into question. *American Cyanamid Co.* v. *FDA,* 606 F. 2d 1307, 1314–1315 (D.C. Cir. 1979). To justify a hearing, HEI would have to present some evidence that suggests that there are significant toxicological or chemical differences between radiolytic products and known natural food components. HEI has failed to present any such evidence and, thus, has not provided a basis for a hearing.

HEI contends that until carcinogenicity and mutagenicity studies are performed on concentrated radiolytic products, as suggested by Epstein and Gofman in a letter to the editor of *Science* (Ref. 17), there is no basis for the wholesale approval of irradiation. Epstein and Gofman stated that, "Stable radiolytic products could be extracted from irradiated food by various aqueous and nonaqueous solvents, which could then be concentrated and subsequently tested."

BFIFC, in its report (Ref. 5, p. 18), explicitly considered testing requirements, including the option of testing extracted and concentrated radiolytic products. Based on its review of the available literature dealing with the identity, amount and potential toxicity of radiolytic products, BFIFC recommended that such testing was not necessary to assure the safety of foods irradiated at doses below 1 kGy or of minor ingredients irradiated at doses below 50 kGy because of the low potential concentration of radiolytic products in such foods. The agency, in the omnibus rule, agreed with the recommendation and concluded that foods irradiated under the conditions of the regulation are safe, and that no additional toxicological testing should be required (51 FR 13376 at 13378).

HEI has not justified a hearing on this conclusion. Epstein and Gofman's letter merely presents a general assertion. HEI has not supported it with any evidence that the levels of radiolytic products formed in food irradiated under the conditions of the regulation would be so high as to require that toxicological testing be done or to call into question FDA's conclusion that foods that have been irradiated are safe. Therefore, HEI has not justified a hearing on this issue under 21 CFR 12.24(b)(2).

Finally, HEI asserts that because FDA did not require long-term animal studies, it is in violation of the act. This is a legal issue. Thus, it cannot serve as a basis for a hearing because a hearing will be granted only on the basis of a substantial issue of fact, not on issues of policy or law (21 CFR 12.24.(b)(1)).

FDA discussed applicable sections of the act in the omnibus rule. The agency stated that, "Section 409 of the act lists the [safety] criteria which must be considered by the agency before a food additive regulation is issued. The statute does not prescribe what safety tests should be performed but leaves that determination to the discretion of scientists." (51 FR 13376). As stated above, FDA's scientists have concluded that foods irradiated at the levels permitted need not be tested toxicologically, and the agency agreed with this conclusion (51 FR 13376 at 13378). HEI has not cited any authority that contradicts FDA's conclusions about the type of data that is necessary to support the approval of the use of a food additive. Therefore, FDA finds that this aspect of HEI's objection is without merit.

C. Animal Feeding Studies

As stated in the previous response, FDA concluded that foods irradiated in accordance with this regulation are safe on the basis of the findings and conclusions of BFIFC, the Task Group, and other information in the agency files.

1. Consideration of Wholesomeness Studies

HEI stated that:

The FDA admits that "useful information has been learned from those feeding studies where there has been some exaggeration of dose relative to that prescribed by this regulation," and argues that such information establishes the safety of food irradiated in accordance with the regulation (51 FR 13382). In a review of 1,223 wholesomeness studies conducted by J. Barna for the Hungarian Academy of Sciences in 1979, study results were classified as either neutral, adverse, or beneficial. Each study could have several outcomes, since studies could address more

than one issue. Barna found 1,414 adverse effects, 185 beneficial effects, and 7,191 neutral effects * * *. A more detailed compilation of adverse effects identified in the Barna study, prepared by [the] Coalition for Alternatives in Nutrition and Healthcare, is attached as Exhibit B. FDA's Irradiated Foods Task Group did not take into account this review of safety studies compiled by J. Barna, despite their objective to "compile and summarize the toxicology data pertaining to irradiated foods." 51 FR 13378 FDA should have considered these studies when reviewing relevant toxicological data, and should not have simply dismissed the adverse evidence. Testimony of scientists regarding this FDA failure will be presented at the public hearing.

(HEI Para. I.16.)

A hearing will not be granted on the basis of mere allegations or general descriptions and contentions (21 CFR 12.24 (b)(2)). HEI must, at a minimum, "raise a material issue concerning which a meaningful hearing might be held". *Pineapple Growers Ass'n of Hawaii* v. *FDA* 673 F. 2d 1083, 1085 (9th Cir. 1982).

HEI alleges, without elaboration or support, that the Task Group did not take into account the review article by Barna (Ref. 18). This statement is belied by the record. The Task Group considered the 1979 Barna article cited by HEI, listed it and all of the available relevant studies cited therein in the bibliography of reports evaluated by the Task Group (Ref. 19), and placed this listing along with the evaluation forms for these studies on public display. Thus, HEI's objection is without merit and is not a basis for a hearing.

HEI also misrepresents the conclusions of Barna's article. Contrary to what HEI implies, Barna did not conclude that the irradiation of food is unsafe. In fact, Barna carefully reviewed the technological, biotechnical, and analytical inadequacies that "* * * may lead to adverse effects * * * which could be mistaken as consequences of radiation treatment * * *" and concluded that "* * * neither beneficial nor adverse effects of irradiated food consumption are consistent, unambiguous and reproducible. Neither of them can be traced back to a given food or group of foods or level of radiation dose." (Ref. 18, p. 205 and p. 266.)

Furthermore, contrary to HEI's allegation, FDA did not dismiss any adverse evidence. The agency stated in the omnibus rule that the Task Group examined in detail all studies that either raised questions concerning the possibility of adverse effects or that appeared to support a conclusion that the irradiated food studied is safe and concluded that studies with irradiated foods do not show adverse toxicological effects (51 FR 13376 at 13378). This review of available toxicology data included an attempt to identify any consistent patterns or trends of adverse effects reported in different studies. The agency found no patterns or trends that would demonstrate that a reported adverse toxicological effect was attributable to irradiation of the food (51 FR 13376 at 13384). HEI has not pointed to specific evidence that FDA either dismissed without cause or misinterpreted in making this finding. Thus, it has failed to justify a hearing.

2. Consideration of Possible Adverse Effects

HEI stated that:

The Irradiated Foods Task Group, which reviewed available toxicological data concerning irradiated foods, examined 69 studies in detail (51 FR 13378). Thirty-two of these 69 studies indicated adverse effects from irradiated foods, yet the Task Group concluded that the studies did not show adverse effects. This cannot be considered "scientific" nor honest. Evidence regarding the Task Group report and the problems associated with it will be presented at the public hearing.

(HEI Para. I.5.)

A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (21 CFR 12.24(b)(2)). HEI must, at a minimum, "raise a material issue concerning which a meaningful hearing might be held." *Pineapple Growers Ass'n of Hawaii* v. *FDA, supra.*

The Task Group examined in detail those studies, referred to above, that appeared on their face to show adverse effects. The Task Group found that because of problems associated with diet or inadequate experimental design, any adverse toxicological effects reported in these studies could not be attributed to irradiation of the food (Ref. 6). In the omnibus rule, FDA noted that it relied on the findings of the Task Group in concluding that foods irradiated under the conditions of the regulation are safe (51 FR 13376 at 13378). HEI has not submitted any specific information from any of the studies to challenge the Task Group's analysis nor cited any evidence that calls into question the safety of foods irradiated under the conditions of the regulation.

A promise to present evidence regarding alleged problems associated with studies reviewed by the Task Group does not provide a sufficient basis on which to grant a hearing. A person requesting a hearing must support its allegations with an adequate proffer of evidence. *General Motors Corp.* v. *FERC,* 656 F.2d 791, 798 n.20 (D.C. Cir. 1981). HEI has failed to make such a proffer on this issue and thus has failed to demonstrate that a hearing is appropriate on whether the Task Group conclusions are correct.

D. Polyploidy

In the omnibus rule, the agency responded to comments claiming that polyploidy (chromosomal changes) had been shown by workers at the National Institute of Nutrition (NIN), Hyderabad, India, to be a toxic consequence in animals and humans of ingestion of irradiated wheat (Ref. 20). The agency cited a summary of a report (51 FR 13376 at 13385) by a scientific committee (hereafter called "the Indian Committee") that was commissioned by the Indian Government to investigate why studies done at NIN were contradicted by studies conducted at the Bhaba Atomic Research Centre (BARC) in Bombay, which showed no adverse effect. The Indian Committee had conducted an indepth review of the data from both laboratories and concluded that there was no evidence that increased polyploidy was associated with ingestion of irradiated wheat (Ref. 21). FDA's Task Group (Ref. 22) reviewed the studies performed at NIN during the 1970's and the findings of the Indian Committee. Based on the Task Group's review and other available evidence, the agency accepted the finding of the Indian Committee that the conclusions reached by investigators at NIN were not supported by the raw data (51 FR 13376 at 13385).

HEI disagreed with FDA's decision, stating:

A study by Bhaskaram, et al, * * * found increased incidence of chromosomal changes (polyploidy) in the blood of malnourished children fed freshly irradiated wheat, and subsequent studies found similar results in test animals. Food irradiation proponents have charged that this study was fraudulent and was repudiated by the National Institute of Nutrition in India which sponsored the study. Relevant correspondence regarding this study is attached as Exhibit C, verifies that the study has not been repudiated by the National Institute of Nutrition, and indicates other studies conducted that relate to this issue. The FDA claims that some unnamed "committee of Indian scientists" has refuted this study, but their refutation does not appear in the refereed scientific literature or in the journal in which the original study appeared (51 FR 13385). The evidence identified in Exhibit C and further evidence supporting the concerns raised by the Bhaskaram study would be presented at the public hearing. In addition, the National Institute of Nutrition replicated the freshly irradiated wheat studies in monkeys and found increased incidence of polyploid cells. VIJAYALAXMI, "Cytogenetic Studies in

Monkeys Fed Irradiated Wheat," *Toxicology* 9: 1978: 181–184. The fact that this study was performed and confirmed the previous findings of Bhaskaram was not mentioned in the FDA final rule. The above evidence and additional evidence will be presented at public hearings.

(HEI Para. I.18.)

HEI's exhibit C contains a copy of the Bhaskaram study with malnourished children (Ref. 20); a copy of a November 14, 1984, memorandum from Martin Welt, Ph.D., to the Executive Director of HEI and other members of a panel discussion on "Alternate Uses—Focus on Food Irradiation," stating that the study may have been fraudulent, that authorities at NIN had repudiated the study, and that an Expert Committee appointed by the International Food Irradiation Project found that the study was without merit; a February 20, 1985, letter from Dr. P.S. Elias of the International Project in the Field of Food Irradiation, stating that the Joint FAO/IAEA/WHO Expert Committee on Food Irradiation (JECFI) considered the Bhaskaram study when it gave full toxicological clearance to irradiation of food up to 10 kGy (1 Mrad); an April 2, 1985, letter from Dr. B.S. Narasinga Rao, Director, NIN, explaining why the NIN studies on irradiated wheat were conducted; and a January 18, 1986, letter from Dr. S.G. Srikantia, former Director of NIN, stating that NIN had not repudiated the Bhaskaram study and listing published studies designed to determine whether irradiated foods cause polyploidy or dominant lethal mutations.

Because HEI stated that it would present further evidence supporting the concerns raised by the Bhaskaram study at a hearing, on February 2, 1987, FDA requested that HEI set forth in detail that further evidence. On March 6, 1987, HEI responded by largely reiterating its objection:

> FDA relied upon an unpublished, unnamed "committee of Indian scientists" who challenged a study published in a refereed scientific journal by Bhaskaram, et al., finding polyploidy in the blood of malnourished children fed wheat *freshly* irradiated at doses legalized by FDA.
>
> Food irradiation promoters suggested that the study was fraudulent during a November 8, 1984 panel on food irradiation at the American Nuclear Society/European Nuclear Society joint meeting held in Washington, DC. A panel member even claimed that the study was repudiated by the director of the Institute conducting the study. We wrote to the Institute, and they responded that they stand behind their study. In fact, similar problems with freshly irradiated wheat have been demonstrated in the blood of both monkeys and mice.

(HEI's emphasis) HEI further stated that:

> * * * FDA cites the "committee" report as having been "presented to the Joint Expert Committee in 1976," although agency personnel later had to retract their claim.
>
> The so-called committee of Indian scientists turned out to be two researchers who submitted a "confidential" report to the Ministry of Health and Family Planning in India. The report was requested because research undertaken by the Bhaba Atomic Research Centre (BARC) reported different results than those found by NIN. BARC was seeking approvals to irradiate food. The two person committee submitted a confidential, unpublished report critical of NIN in 1976, and NIN responded with a confidential report to the Indian Government verifying the validity of their work and refuting in detail the claims and conclusions of the critical report. They also included independent evaluations of their data by two of the country's [India's] foremost cytogeneticists. Additional correspondence regarding this issue is attached.

(HEI March 6, 1987, response, p. 8 (Ref. 2).)

HEI also stated that it felt that studies on dominant lethal mutations that were cited in Dr. Srikantia's letter submitted in support of its original objection should be addressed; cited a study by Hickman, et. al., "Rat Feeding Studies on Wheat Treated with Gamma-Radiation I. Reproduction" (Ref. 23) as a disturbing finding that suggests the need for further research in these areas; and cited a passage from Conning, "Evaluation of the Irradiation of Animal Feedstuffs" (Ref. 24) which refers to a study on the effect of an irradiated diet on lymphocyte number.

The "additional correspondence" attached to the March 6th submission consisted of a letter from the Coalition to Stop Food Irradiation (CSFI) to Food Chemical News, a trade newspaper, explaining CSFI's understanding of the history of the Indian Committee report, with enclosures. The enclosures consisted of a letter from FDA to CSFI providing documentation on how FDA received the summary report of the Indian Committee and correspondence between Dr. S.G. Srikantia, former Director of NIN, and Professor J. Schubert of Michigan State University, concerning whether the NIN study was described as fraudulent by members of the November 8, 1984, panel.

The objection, and the attached correspondence, appear to address several subjects, many of which are not related to the finding of polyploidy. The agency will address the polyploidy question first, then deal with all other studies not related to polyploidy but cited in this objection.

1. Allegations That NIN Study Is Fraudulent

First, HEI challenges allegations that the Bhaskaram study was fraudulent. However, such allegations are not an issue in this rulemaking. FDA did not base its conclusion on a finding that the data were fraudulent. FDA concluded in the final rule that the available data from NIN did not provide an appropriate basis on which to conclude that increased polyploidy was caused by ingesting irradiated wheat. Thus, a hearing need not be granted on whether these studies are fraudulent.

2. Whether NIN Has Refuted the Conclusions of the Indian Committee and the Significance of That Fact

Second, HEI argued that certain individuals do not accept the conclusions of the Indian Committee appointed by the Indian Ministry of Health and Family Planning to resolve the question of whether polyploidy is caused by eating freshly irradiated wheat. HEI stated that NIN responded to the Indian Government in a document that verifies the validity of the NIN studies and that refutes the Indian Committee report in detail. However, neither HEI nor anyone else has submitted this document to FDA. HEI thus implies that data or analyses not seen by FDA could resolve this issue in its favor.

The person seeking a hearing must meet a threshold burden of tendering evidence that suggests the need for a hearing. *Costle* v. *Pacific Legal Foundation, supra,* 445 U.S. at 214. To justify a hearing, HEI would have had to submit the NIN response or some other evidence that challenges the findings and conclusions of the Indian Committee and that would cause the agency to change its conclusion.[1] HEI

[1] FDA received a letter, dated September 26, 1986, from Dr. Srikantia, Director of NIN when the Bhaskaram study was conducted, stating that the Indian Committee report was a confidential document submitted to the Government of India at the Government's request. He said that he had submitted a reply to the Government, and that two well-known cytogeneticists had examined NIN's data in depth and had agreed with NIN's findings. FDA wrote to Dr. Srikantia on October 27, 1986, and November 24, 1986, stating that FDA was not aware of his rebuttal and invited him to submit any information to FDA that would be relevant to the issue raised by objections. Dr. Srikantia replied on December 16, 1986, but did not submit a copy of his rebuttal to the Indian Committee or of any other report. Instead, he simply stated that he disagreed with the report of the Indian Committee; that many would agree that the polyploidy studies were of good design; that two well-known cytogeneticists in India independently reviewed NIN's work on polyploidy in children, monkeys, and rats and have agreed with its conclusions; and that NIN's

Continued

has not submitted any such evidence. Thus, HEI has not provided a basis for a hearing.

3. Citation of Indian Committee Report

HEI's third point is that FDA made an error in the way in which it cited the Indian Committee report.[2] FDA agrees that it incorrectly cited this report as a "Report Submitted to the Joint FAO/IAEA/WHO Expert Committee on the Wholesomeness of Irradiated Food, 1976" (51 FR 13376 at 13398). HEI is correct that the committee report was commissioned by the Ministry of Health and Family Planning in India to determine why results from the BARC differed from those reported by NIN.

However, FDA's error in citing this report did not affect the availability of this information. The agency placed a copy of the report summary on public file with the other references. The incorrect citation also did not change the report's conclusions, the validity of its conclusions, or the validity of the agency's conclusions based on that report. Therefore, because the agency's miscitation of the report did not affect the proceeding in any material way, and because HEI has not alleged that it did, the miscitation does not provide a basis for granting a hearing (21 CFR 12.24(b)(4)).

4. The Monkey Study

Fourth, HEI states that Vijayalaxmi, at NIN, replicated the freshly irradiated wheat studies in monkeys and found increased incidence of polyploid cells (Ref. 25), thus confirming the previous findings of Bhaskaram.

A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (21 CFR 12.24(b)(2)). HEI must, at a minimum, "raise a material issue concerning which a meaningful hearing might be held." *Pineapple Growers Ass'n of Hawaii* v. *FDA, supra.* Although FDA did not explicitly cite the monkey study in the omnibus rule, the administrative record shows that this study was among the NIN studies that the Task Group and FDA considered. The agency based its conclusion on the findings of the Task Group and on the other information in the administrative record (51 FR 13376 at 13378). The Task Group concluded (Ref. 22) that *none* of the studies on polyploidy done at NIN, including those reported both by Bhaskaram (Ref. 20) and Vijayalaxmi (Ref. 25, 26, and 27), was reliable.

A person seeking a hearing must meet a threshold burden of tendering evidence that suggests the need for a hearing. *Costle* v. *Pacific Legal Foundation, supra,* 445 U.S. at 214. To justify a hearing, HEI would have had to submit some evidence that challenges the conclusion that all the NIN studies were not reliable. For example, this standard could have been met if HEI had provided evidence that the monkey study was designed to correct the problems with the earlier NIN studies that were noted by the Indian Committee and by the agency (Ref. 22) or had provided evidence that the design of the NIN studies was not flawed. HEI, however, has failed to proffer any such evidence and thus has not provided any basis to justify a hearing on this objection.

5. Letter From Dr. Srikantia

Dr. Srikantia's January 18, 1986, letter to HEI stated that NIN had not repudiated the Bhaskaram study.

FDA did not state that NIN had repudiated the study, nor did it base its conclusion on a finding that the data were repudiated by NIN. Such an allegation is not an issue in this rulemaking. FDA concluded in the final rule that the available data from NIN did not provide an appropriate basis on which to conclude that increased polyploidy was caused by ingesting irradiated wheat.

Dr. Srikantia's letter referred to reports on studies designed to detect polyploidy, including three reports other than those performed at NIN (Ref. 29, 30, and 31). Two of the cited reports (Refs. 29 and 30) did not find increased polyploidy in the cells of animals fed irradiated food or freshly irradiated diets. One of these two reported the results of six in vivo genetic toxicity tests using three different irradiated foods: fish, dates, and chicken (Ref. 29). The tests were as follows: sex-linked recessive lethal mutations in *Drosophila* (dried dates only); chromosome aberrations in bone marrow of Chinese hamsters; micronucleus test in rats, mice, and Chinese hamsters; sisterchromatid exchange to bone marrow of mice and Chinese hamsters, as well as in spermatogonia of mice; and DNA metabolism in spleen cells of Chinese hamsters. The authors concluded that none of the tests provided any evidence of genetic toxicity. The agency had reviewed preliminary reports of some of these tests and referenced them in the omnibus rule (51 FR 13376 at 13397) and in the administrative file (81N-0004). The second study (Ref. 30) did not find an increase in frequency of polyploid cells in the bone marrow of rats fed irradiated wheat. The agency had reviewed this study and listed it in the administrative file.

In the third report cited, Renner (Ref. 31) concluded that "(f)eeding a standard diet freshly irradiated with high doses (>3 Mrads) has a transitory effect in the bone marrow of Chinese hamsters as evidenced by an increased incidence of polyploid cells" but that "there is no

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observation that polyploidy in children quickly disappeared after cessation of feeding with freshly irradiated wheat was not at variance with biological possibilities. He also reiterated NIN's position that wheat subjected to irradiation must be stored for 3 months to be safe for consumption. He stated that just because wheat is likely to be stored for even longer periods does not negate NIN's findings on freshly irradiated wheat.

[2] Because of the controversy over the mutually contradictory findings at two Government laboratories, the Indian Ministry of Health and Family Planning appointed a committee of two University scientists (Indian Committee) to identify the cause of the discrepancy between the data from these two groups. The Indian Committee (Ref. 21) critically examined the data from both laboratories and concluded that an important reason for the conclusion regarding increased polyploidy was the abnormally low frequency of polyploidy (0.0 percent) in the cells of children not eating irradiated wheat (Ref. 20). The Indian Committee also stated that cells from the malnourished children at the beginning of the study exhibited a fuzzy appearance and could not be counted properly. They concluded that the frequency of 1.8 percent polyploid cells found in children eating freshly irradiated wheat was well within the normal range of healthy human beings.

The Indian Committee also examined studies by Vijayalaxmi reporting polyploidy in rats and mice fed freshly irradiated wheat. They evaluated the techniques used by NIN workers to determine the fraction of polyploid cells and found that the method used yielded highly variable and unreproducible results. They concluded that the differences between Vijayalaxmi's findings and those of researchers at BARC "mainly lie in the faulty and biased selection of the sample" and that "the results from animals fed freshly irradiated wheat are compatible with those from animals fed unirradiated wheat." The Indian Committee did not consider the monkey study, which was published after the Indian Committee report; however, there is no evidence that the Vijayalaxmi study in monkeys was designed to overcome the serious problems of faulty and biased selection of the sample noted by the Indian Committee in the two earlier studies by the same author.

The 1976 meeting of the Joint FAO/IAEA/WHO Expert Committee on Food Irradiation (JECFI) in Geneva, Switzerland considered the question of polyploidy. JECFI noted the contradictory results of different investigators (Ref. 28). They also noted that the significance of observations of polyploidy are unclear because the range of the observations of the incidence of polyploidy varies considerably between normal groups of the same species of animal, and that the toxicological implications of an increased incidence of polyploidy are not understood. However, they concluded that resolution of the contradictory conclusions was not necessary because the studies on freshly irradiated wheat were not relevant to actual practice considering that wheat is usually stored longer than 12 weeks; and no increase in polyploidy was reported by any investigator, including those at NIN, for wheat stored 12 weeks after irradiation. They recommended unconditional acceptance of wheat and ground wheat products irradiated for the purpose of disinfestation to a maximum dose of 1 kGy (100 krad) and did not recommend an explicit storage requirement. Dr. Srikantia, the Director of NIN, was a member of the JECFI that made this recommendation.

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evidence for any mutagenic effect being produced as a result of feeding an irradiated diet." He noted that the irradiation dose required for insect disinfestation is less than 100 kilorads, and no effects on polyploidy incidence were seen at doses below 2,000 kilorads (2 Mrad). Thus, this study does not provide evidence that polyploidy occurs in animals fed food irradiated under conditions of the regulation. HEI has not explained why this study supports its contention or cited any study other than those conducted at NIN that has reported an association between eating food freshly irradiated at a dose permitted under the regulation and polyploidy. Thus, HEI has failed to provide a basis for a hearing.

Dr. Srikantia's letter also cited seven studies on dominant lethal mutations, two of which reported an effect and five of which reported no effect. FDA discussed the two studies on dominant lethal mutations that reported an effect in the omnibus rule (51 FR 13376 at 13385 and 13387) and concluded that one study, conducted at NIN, was unreliable, and that the observations in the other study were not evidence of dominant lethal mutation and could not be reproduced in three comparable studies. (See also the section on "Dominant Lethal Tests.") Neither HEI nor Dr. Srikantia has proffered any evidence or explanation that challenges or calls into question the agency's analysis of these studies. Nor has HEI provided any explanation of why it considers studies on dominant lethal mutations to be relevant to polyploidy. Therefore, HEI has not provided a basis for a hearing on this question.

6. Hickman Study

In its March 6, 1987, letter HEI stated that a study by Hickman et al. (Ref. 23):

> * * * concluded that wheat irradiated at least 2 to 5 weeks before feeding showed no adverse reproductive effects. Yet the study tables reveal that twice as many stillbirth[s] occurred in those fed wheat irradiated at 200 krad compared to the control. Four litters in the 200 krad irradiated wheat group were stillborn, compared to one in the control group. Such disturbing findings suggest the need for further research in these areas.

(HEI March 6, 1987, response, p. 9 (Ref. 2).)

The Hickman study investigated whether reproductive effects are caused by feeding wheat treated with gamma radiation to rats and does not discuss polyploidy. The authors of the study concluded that this study showed no adverse effects. The number of stillbirths in the high dose group, though higher than the concurrent controls, was still within the normal range for this rat colony. Moreover, the number of stillbirths in the group fed wheat irradiated at a dose permitted by the omnibus rule was less than that of the concurrent controls. The agency agreed that the authors' conclusions were valid and referenced this study in the omnibus rule (51 FR 13376 at 13386). HEI has not provided any basis on which to challenge the conclusions of the authors and of FDA. Nor has HEI proffered any evidence to relate this study to polyploidy. Instead, HEI has merely suggested that such findings indicate a need for further research in these areas. A hearing will not be granted on the basis of mere allegations or contentions (21 CFR 12.24(b)(2)). Thus, HEI's reference to the Hickman study does not provide a basis for a hearing.

7. Conning Review

Finally, in its March 6, 1987 letter, HEI stated that:

> Conning, D.M., "Evaluation of the Irradiation of Animal Feedstuffs," in P.S. Elias and A.J. Cohen, ed's, RECENT ADVANCES IN FOOD IRRADIATION, 247 at 263 (1983) cites a study by Ehrenber. [sic] L. et al which found a 15 to 20 percent reduction in the lymphocyte count in male Sprague-Dawley rats, whether fed within 96 hours of irradiation or after storage for up to 1 year. Lymphocytopenia was produced by all diets irradiated at or above 6 kGy. Conning notes at page 268: "The agents responsible for the lymphocytopenia induced by irradiated laboratory diets have not been identified or their mechanism of action satisfactorily explained. There appears to be no published work that contradicts these findings, the various studies by Huismans being inadequate in a number of respects. A possible effect on the immune system has still not been ruled out and further carefully-controlled experiments in this area using adult animals are warranted, particularly in the light of the Russian study which indicated that long-term feeding of an irradiated diet produces kidney damage possibly by an immunological mechanism."

(March 6, 1987, response, p. 9 (Ref. 2).)

In his review, Conning (Ref. 24) cited two studies by Ehrenberg and colleagues (Ref. 32 and 33). One of these studies (Ref. 32) reported that lymphocytopenia was produced by feeding diets irradiated at or above 6 kGy, but not at 2 kGy. The other study (Ref. 33) reported a 15 to 20 percent reduction in lymphocyte counts in rats fed diets irradiated at 30 to 90 kGy. As Conning stated, " * * * the effect was at the limit of detection, a 60 kGy irradiated diet resulting in only a 7% reduction in the lymphocyte number" (Ref. 24).

HEI has not provided any reason for considering these studies relevant to its objection that irradiated food causes polyploidy. Further, the effects reported in these studies are not relevant to the uses of irradiation permitted under the conditions of the regulation, which limits irradiation of foods other than minor ingredients to a dose not exceeding 1 kGy. HEI has not provided any basis for finding that studies with food irradiated at such exaggerated doses have any relevance to the safety of food irradiated under the conditions set forth in 21 CFR 179.26. Thus, this aspect of HEI's objection does not provide a basis for a hearing.

Moreover, FDA's Task Group considered these studies and determined that they suffered from such serious methodological deficiencies that no valid conclusions could be drawn on the basis of the data from them (Ref. 19). HEI has not contested this determination. Nor did other feeding studies reviewed by the agency show a similar effect.

The long-term rat feeding study done in the Soviet Union and referred to by Conning is also unrelated to polyploidy. The authors of the study reported damage to kidneys and testes in rats fed irradiated feed. The agency addressed this study in a response to a comment on the omnibus rule (51 FR 13376 at 13386) and concluded that because of the lack of data in available reports on this study, in contrast to the considerable amount of data that FDA had from other studies that showed no effects, the results described in these Soviet Union reports did not raise substantial questions about the safety of food irradiated under the conditions of this regulation (51 FR at 13376 at 13386). (This study is discussed elsewhere in the document. See section II. E. "Studies Reporting Effects on Kidney and Testes.") HEI has not provided any basis, nor cited any evidence, that would call the agency's conclusion into question. Thus, it has failed to justify a hearing on this aspect of the objection.

In sum, HEI's reference to Conning and the studies that Conning cites in his review article does not justify a hearing on polyploidy because HEI has not provided any basis for considering these studies relevant to polyploidy. In addition, FDA had considered virtually all of the studies cited by Conning and found them not to provide a reliable basis on which to make conclusions about the safety of the uses of food irradiation at issue in this proceeding. HEI has not challenged these findings.

Thus, HEI has merely disagreed with the agency's conclusion that the studies conducted at NIN in India do not provide a basis on which to find that adverse effects would be caused by ingestion of irradiated foods and has not

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provided any evidence that would challenge the findings of the Indian Committee or the analysis of the agency. Instead, HEI has submitted letters from persons associated with the studies that say that they have not retracted their work and has referred to other studies unrelated to polyploidy. HEI has not proffered any evidence to show that polyploidy is a true adverse effect from ingestion of irradiated food that should be considered further by the agency. Thus, HEI's objection consists of mere allegations and contentions and of references to data previously considered by the agency that do not challenge the agency's conclusion. Consequently, the objection does not provide an adequate basis for a hearing.

8. FDA's Consideration of Scientific Evidence

In another assertion, related to the Bhaskaram study, HEI stated that:

> The FDA argues that animal testing is not always necessary to declare a food additive or process safe, where by "sound reasoning" it can determine otherwise (51 FR 13382). The FDA goes on to dismiss animal testing data which indicates hazards from consuming irradiated food, which cannot be considered the use of "sound reasoning." Animal testing was not "too insensitive to show an effect from irradiation of food at the doses allowed," in some studies, such as the study by Bhaskaram et al. "Effects of feeding irradiated wheat to malnourished children," 28 THE AMERICAN JOURNAL OF CLINICAL NUTRITION 130 (Feb. 1975). This study found blood abnormalities in malnourished children fed freshly irradiated wheat. This is but one example of FDA's failure to protect public health by acting on evidence of harm from food irradiation. If ignoring scientific studies indicating harm is FDA's "sound reasoning," then FDA is incapable of "sound reasoning." Further evidence regarding this issue will be presented at the public hearing, including additional scientific studies and testimony by scientists.

(HEI Para. I.15.)

The agency asked HEI on February 2, 1987, to set forth in detail the factual information and analysis that it intended to present at a hearing.

On March 6, 1987, HEI stated:

> The FDA assumption that doses of 100,000 rads will not create any harmful effects in food was not based upon the scientific animal feeding literature or other documented research. It should be characterized as a hope or a theory, rather than as a fact. Dr. Donald Louria is in the process of reviewing the five studies considered by a 1982 FDA panel as "adequate" to support the safety of irradiated foods. Two of the five studies reviewed thus far suffer flaws, according to Dr. Louria. We are now asking other scientists to review these studies, now that they have been identified.

(HEI March 6, 1987, response, p. 6 (Ref. 2).)

A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (21 CFR 12.24(b)(2)). HEI must, at a minimum, "raise a material issue concerning which a meaningful hearing might be held." *Pineapple Growers Ass'n of Hawaii* v. *FDA*, supra.

In this objection, HEI alleges that FDA has dismissed animal testing data that indicate that there is a hazard from irradiated foods and has ignored scientific evidence. To justify a hearing on these assertions, HEI must point to some evidence that FDA did not consider that would challenge the conclusions of the agency or that shows that the agency has not correctly analyzed testing data. The only specific evidence that HEI has pointed to in support of its allegations is the Bhaskaram study (Ref. 20). HEI's objection must provide at least a plausible basis on which to find that FDA is incorrect in finding that this study is unreliable. As the discussion in the preceding section makes clear, however, HEI has failed to do so. Thus, the objector has not met its "threshold burden of tendering evidence suggesting the need for a hearing." (See *Costle* v. *Pacific Legal Foundation*, supra.)

Moreover, a hearing will not be granted on factual issues that are not determinative with respect to the action requested (21 FR 12.24(b)(4)). Even if the agency agreed that two of the five studies referred to by HEI in its March 6, 1987, submission suffer flaws, this fact would not change the agency's conclusion that there is an adequate margin of safety for foods irradiated under the conditions of the regulation. Although the agency found that the studies in question were supportive of its conclusion on safety, those studies were not the primary basis for FDA's conclusion that foods irradiated under the conditions of the regulation are safe. FDA's conclusion was based on its review of all available evidence, including the findings, rationale, and conclusion of BFIFC and of the Task Group (51 FR 13376 at 13378). HEI has not proffered any evidence that would call this evidence into question. Thus, HEI has not justified a hearing.

HEI promised to present additional scientific studies and testimony by Dr. Donald Louria or other scientists at a hearing but did not specify what evidence it would present. A hearing cannot be justified on the basis of a promise that some unidentified evidence will be provided at the time of that hearing. A person seeking a hearing must meet a threshold burden of tendering evidence that suggests the need for a hearing. *Costle* v. *Pacific Legal Foundation, supra,* 445 U.S. at 214. Because HEI failed to submit the promised scientific reviews and to specify the evidence it would present at a hearing, FDA has no way of determining whether this evidence justifies a hearing. Therefore, HEI has failed to meet its threshold burden.

E. Studies Reporting Effects on Kidney and Testes

In the spring of 1984, the U.S. Department of Agriculture (USDA) submitted to FDA several reports of studies conducted with radiation-sterilized chicken (hereafter referred to as "the Raltech studies") (49 FR 40623; October 17, 1984). These studies were conducted to test the safety of chicken irradiated in the frozen state, in the absence of air, at sterilizing doses. The food tested and the conditions of irradiation were totally different from those that FDA proposed to permit. Nonetheless, the agency received several comments on its omnibus proposal alleging that effects on the kidneys and testes, and on the survival of mice in one of these studies, showed that foods irradiated under the conditions of the proposal had not been shown to be safe (51 FR 13376 at 13386). Although these studies were not directly relevant to the safety evaluation of the irradiated foods permitted by this rule, FDA thoroughly evaluated them to determine whether any adverse effects had been demonstrated that would raise new safety questions or that would challenge the basis of FDA's analysis. FDA found that no adverse effects had been shown that could be attributed to irradiation of the food (50 FR 29658). The adverse effects noted appeared to be attributable either to chance occurrence or to giving mice such a high proportion of chicken meat in the diet. FDA concluded that these studies provided no information that would cast doubt on the safety of the foods that could be irradiated under either the pork rule (50 FR 29658) or the omnibus rule (51 FR 13376 at 13386).

In the omnibus final rule, FDA also responded to comments concerning a study done in the Soviet Union that reported damage to kidneys and testes of rats fed irradiated lab chow. The agency concluded that the data reported in the two available reports on this study are inadequate to conclude that irradiation of the diet caused adverse effects, and that, considering the far larger amount of data from other similar studies that showed no effects, these reports did not raise substantial

questions about the safety of food irradiated under the conditions of this regulation (51 FR 13376 at 13386).

1. Objection to omnibus rule

HEI stated:

The FDA stated that one comment noted increased kidney damage in the Raltech irradiated chicken studies (51 FR 13386), and the FDA did not address this concern in item no. 33. [Comment 33 in the omnibus rule.] In item no. 34, the FDA cited two Russian reports that found damage to kidneys and testes in rats fed irradiated feed, but dismissed these studies. Evidence regarding the studies which FDA chose to uphold and evidence regarding the original studies, so that the FDA conclusions can be evaluated properly, would be presented at the public hearing. (HEI Para. I.21.)

Further, HEI stated that:

The FDA cites a report prepared by Raltech scientists which was reviewed by Donald W. Thayer, Chief of the Food Safety Laboratory of the Eastern Regional Research Center of the Department of Agriculture in SUMMARY OF SUPPORTING DOCUMENTS FOR WHOLESOMENESS STUDIES OF PRECOOKED (ENZYME INACTIVATED) CHICKEN PRODUCTS IN VACUUM SEALED CONTAINERS EXPOSED TO DOSES OF IONIZING RADIATION SUFFICIENT TO ACHIEVE "COMMERCIAL STERILITY" (51 FR 13386)[.] Dr. Thayer concluded that "two of the studies namely the dominant lethal study and the chronic toxicity, oncogenicity, multigeneration reproductive study with mice had some possibly adverse findings which will require careful consideration before the process can be declared safe" (at page 9)[.] The Agency concluded that independent examination of the lesions did not support classification of the lesions as carcinogenic, but the FDA fails to explain the increased deaths in the study group fed gamma irradiated chicken. Further testimony regarding this study would be offered at a public hearing. (HEI Para. I.20.)

FDA asked HEI on February 2, 1987, to set forth in detail the factual information that it intended to present at a hearing. On March 6, 1987, the objector responded by stating that:

Dr. Donald Louria, New Jersey College of Medicine, will be asked to comment on the validity of the original research study on kidney damage and testes, and to explain whether other studies refute the studies suggesting damage or whether these studies differ from those showing damage. (HEI March 6, 1987, response, p. 11 (Ref. 2).)

Although HEI stated its disagreement with FDA's evaluation of the Raltech studies of mice fed radiation-sterilized chicken, it has not identified any evidence that would call into question any of the agency's conclusions. HEI has not identified any evidence, nor offered any reason, that would provide a basis on which to find that a study on radiation-sterilized chicken is relevant to a rule that does not permit either the irradiation of food at the levels necessary to sterilize chicken or the irradiation of chicken.

As discussed in the omnibus rule, the agency concluded that the decreased survival in the female mice was not treatment-related because it occurred in only one sex group, and because the decrease was only marginal (51 FR 13376 at 13386). HEI has not proffered any evidence to challenge this conclusion. Rather, HEI simply asserts that further testimony regarding this study would be offered at a hearing. A hearing cannot be justified on the basis of a promise that some unidentified evidence will be provided at the time of that hearing. The person seeking a hearing must meet a threshold burden of tendering evidence that supports the need for a hearing. *Costle* v. *Pacific Legal Foundation*, supra, 445 U.S. at 214. HEI has failed to meet that threshold. Therefore, a hearing on this objection is denied.

Moreover, the agency noted that mice in all groups fed chicken meat (both nonirradiated and irradiated) showed signs of kidney damage (51 FR 13376 at 13386). The incidence of this effect was far higher in the mice fed frozen nonirradiated chicken than in either of the groups fed irradiated chicken. Therefore, the agency concluded that the effects were the result of the high protein content of the chicken diets rather than of the irradiation of some diets (51 FR 13376 at 13386). HEI has not proffered any evidence to challenge this conclusion.

Nor has HEI identified any specific, reliable evidence that would challenge FDA's conclusion that the reported results of the Soviet Union rat study were not supported by data and were contradicted by other studies. As FDA stated in the omnibus rule (51 FR 13376 at 13386), critical information necessary to verify that the reported effects are treatment related is not available. It is the objector's burden to come forward with evidence that would show that the agency's analysis is incorrect. *American Cyanamid Co.* v. *FDA*, supra, 606 F.2d at 1314–1315. HEI has not met this burden.

The agency attempted to obtain the raw data from the study done in the Soviet Union through several sources but could not obtain such information. The Counselor, Foreign Affairs Administration, Soviet Ministry of Health responded to FDA's request by stating that "the indicated materials are the intellectual property of the authors of the experiment and cannot be forwarded to the Administration's scientists" (Ref. 34).

As for Dr. Thayer's statement, HEI stated:

Dr. Thayer concluded that "two of the studies namely the dominant lethal study and the chronic toxicity, oncogenicity, multigeneration reproductive study with mice had some possibly adverse findings which will require careful consideration before the process can be declared safe."

This statement was drawn by HEI, somewhat out of context, from a report to FDA (Ref. 35) by USDA that summarized the studies on radiation-sterilized chicken that it was submitting to FDA. Dr. Thayer's complete statement was:

On balance these studies supported the conclusion that the irradiation sterilized chicken products were wholesome, however, two of the studies namely the dominant lethal study and the chronic toxicity, oncogenicity, multigeneration reproductive study with mice had some possibly adverse findings which will require careful consideration before the process can be declared safe. (Ref. 35, p. 9.)

Thus, Dr. Thayer's statement merely alerted FDA to review these studies more fully.

As discussed above, the agency did review the Raltech mouse study and found no effects on mice that could be attributed to the consumption of irradiated food. Furthermore, in the summary report, Dr. Thayer went on to discuss the reason for highlighting the dominant lethal study. He stated:

There was no evidence that any of the diets induced dominant lethal effects in mice which ate chicken as 35% of the total diet; however, again the positive control, in this case triethylenemelamine, did not induce lethal mutations in spermatid and spermatozoan stages of spermatogenesis in mice * * *. (Ref. 33, p. 22.)

Dr. Thayer was pointing out that this dominant lethal study would not be considered a valid study in determining the safety of radiation-sterilized chicken. However, even if this study were valid, it would not justify a hearing because, as stated earlier, the Raltech studies on radiation-sterilized chicken are not relevant to this omnibus rulemaking.

Thus, the Thayer report cited by HEI does not support HEI's contention that irradiated food is unsafe. Because HEI has not proffered any other evidence that supports its general contention, it has failed to meet the threshold burden of tendering evidence that suggests that there is a need for a hearing on this issue (see *Costle* v. *Pacific Legal Foundation*, supra, and (21 CFR 12.24(b)(2)).

HEI has also stated that Dr. Louria will be asked to comment on the validity of the "original research study." A

hearing cannot be granted on a mere statement that someone will testify about the validity of a study without a proffer as to what that person will testify to that demonstrates that there is a genuine and substantial issue of fact that provides a basis for a hearing. Thus, a hearing on this objection is denied.

2. Objection to irradiated pork rule

Public Citizen Health Research Group (HRG), in its objection to the irradiated pork rule, also argued that FDA's dismissal of increased testicular tumors in the radiation sterilized chicken study was inappropriate in light of the Soviet Union report on damage to the testes. HRG did not indicate that it intended to present any evidence at a hearing, however.

To justify a hearing, a challenge to an agency's factual conclusion must present a live controversy. *Community Nutrition Institute* v. *Young,* supra, 773 F.2d at 1364. In addition, the objection must raise a material issue concerning which a meaningful hearing might be held. *Pineapple Growers Ass'n* v. *FDA,* supra, 673 F.2d at 1085. HRG's objection fails to meet these requirements.

HRG's objection to the irradiated pork rule appears to draw upon a comment that FDA received in the omnibus rulemaking concerning the rat study conducted in the Soviet Union. At the time of HRG's objection, FDA had not fully considered this comment.

Ultimately, FDA decided, as it explained in the final rule in the omnibus proceeding (51 FR 13376 at 13386), that the Soviet reports lacked critical information necessary for proper evaluation of the study. The burden then shifted to HRG to maintain the viability of its objection by proffering some information that called into question the agency's conclusion on this study. However, HRG failed to submit an objection to the agency's conclusion.

As a result, there is no reason to hold a hearing on this objection because there is no live controversy and thus no material issue on which a hearing could be held. In the absence of some explanation from HRG for why the Soviet Union reports on the rat study are valid in spite of the deficiencies cited by the agency, or for why the agency was wrong in finding that there were deficiencies, it is undisputed that those reports do not provide an appropriate basis on which to question the safety of pork irradiated in accordance with the irradiated pork regulation. Therefore, the information submitted by HRG does not justify the factual determination urged, and FDA is denying HRG's request for a hearing on this issue under 21 CFR 12.24(b)(3).

Moreover, the agency carefully considered the possibility of a treatment-related incidence of testicular tumors in the radiation-sterilized chicken study. As discussed in the irradiated pork rule and the omnibus rule, agency scientists examined the histology slides and concluded that the evidence did not support a treatment-related induction of testicular tumors (50 FR 29658; 51 FR 13376 at 13386). HRG did not submit any evidence that would call the agency's evaluation of the histology slides into question.

F. Alleged Effects on Fertility

As discussed above, FDA reviewed and evaluated all available animal feeding studies, including reproduction studies, and placed a list of such studies along with the results of its review on public file as references in its omnibus rule (51 FR 13376 at 13397).

The agency made clear in the omnibus rule that, based on the Task Group's examination of all the data, FDA concluded that studies with irradiated foods do not show adverse toxicological effects (51 FR 13376 at 13378; Ref. 36).

HEI stated that,

> Fertility effects of eating irradiated foods are addressed by the FDA (51 FR 13387 [sic]), which chose to ignore studies finding adverse impacts. Critiques of the studies dismissed by the FDA along with critiques of the studies accepted by the FDA would be presented at a public hearing on the issue. (HEI Para. I.22.)

A hearing will not be granted on mere allegations (21 CFR 12.24(b)(2)). In this objection, HEI has not met its "threshold burden of tendering evidence suggesting the need for a hearing." *Costle* v. *Pacific Legal Foundation,* supra, 445 U.S. 198, 214 (1980). HEI alleges that the agency ignored studies that found that consumption of irradiated food had an adverse impact on fertility but has not cited or identified a single such study. Thus, HEI's objection consists of the bald assertion that the agency ignored studies that found an adverse impact on fertility. Without a proffer of evidence to support this assertion, HEI has not justified a hearing (21 CFR 12.24(b)(2).)

G. Early Studies on Irradiated Bacon

As discussed in the omnibus rule (51 FR 13376 at 13384), FDA issued a regulation in 1963 to permit radiation sterilization of bacon based on summaries of feeding studies submitted in a petition (28 FR 1456; February 15, 1963). However, following evaluation of the complete reports of these studies, FDA concluded that the sponsor had not met its burden for demonstrating safety (33 FR 12055; August 24, 1968) and revoked the bacon regulation (33 FR 15416; October 17, 1968).

Objections to the irradiated pork rule stated that FDA should not have issued the irradiated pork regulation because of these studies on irradiated bacon. Some objections noted that these earlier studies caused FDA to revoke its regulation on irradiated bacon. Two of these objections requested a hearing. In the most complete discussion of this issue, HRG stated that:

> In 1963, in response to a petition from the Army, the FDA approved the irradiation for canned bacon. However, in 1968, the FDA rescinded this approval after it reviewed the studies upon which this approval was based and found that they raised doubts about the safety of irradiated bacon * * *. So far as we know, this conclusion has never been reversed. However, before FDA can state that irradiated bacon, or other pork products, are safe, the conclusions from 1968 must be addressed. (Objection No. 27 by HRG, p. 2 (Ref. 37).)

HRG's objection to the irradiated pork rule appears to draw upon a comment that FDA received in the omnibus rulemaking concerning the revocation of the bacon regulation. At the time of HRG's objection, FDA had not fully considered this comment. As it explained in the final rule in the omnibus proceeding (51 FR 13376 at 13384), the agency reconsidered its 1968 action and concluded that the data on radiation-sterilized bacon are of such poor quality that they were inadequate to demonstrate either safety or adverse effects (51 FR 13376 at 13384). The burden then shifted to HRG and the other objectors to maintain the viability of this objection by proffering some information that called into question the agency's conclusion. However, HRG and the other objectors did not object to the agency's discussion and resolution of this issue in the omnibus rule.

As a result, there is no reason to hold a hearing on this objection because there is no live controversy and thus no material issue on which a hearing could be held. In the absence of some explanation from HRG or the other objectors for why the irradiated bacon reports are valid in spite of the deficiencies cited by the agency, or for why the agency was wrong in finding that there were deficiencies, it is undisputed that those reports do not provide an appropriate basis on which to question the safety of pork irradiated in accordance with the irradiated pork regulation. Therefore, the information submitted by HRG does not justify the factual determination urged, and FDA is denying HRG's request for a hearing on this issue under 21 CFR 12.24(b)(3).

Moreover, the agency did not consider it necessary to discuss irradiated

canned bacon in the irradiated pork rule because radiation-sterilized canned bacon is not relevant to the irradiation of fresh pork to control *Trichinella spiralis*. Radiation-sterilized canned bacon, irradiated at doses of 27.9 kGy and 55.8 kGy, is a significantly different product than fresh pork irradiated at doses between 0.3 and 1.0 kGy, as permitted in the July 22, 1985, regulation. A person requesting a hearing must support its allegations with an adequate proffer of evidence. *General Motors Corp.* v. *FERC*, 656 F.2d 791, 798 n.20 (D.C. Cir. 1981). HRG and the other objectors have not proffered any evidence or explanation as to why radiation-sterilized canned bacon has any relevance to the safety of fresh pork irradiated under the conditions set forth in 21 CFR 179.26. Thus, they have failed to provide a basis on which a hearing could be held.

H. Drosophila Study

In the omnibus rule, FDA responded to a comment alleging that a mutagenicity (sex-linked recessive lethal) study in fruit flies (*Drosophila*) raised on radiation-sterilized chicken meat showed an effect consistent with chromosomal damage (51 FR 13376 at 13386). The study (Ref. 38) showed no evidence of mutagenicity. However, the authors of the study also reported data that showed fewer offspring in all groups raised on chicken meat, as compared to those raised on the standard diet for fruit flies, with the fewest offspring in the groups raised on irradiated diets. The agency concluded that this effect could occur for a number of reasons unrelated to reproductive toxicity, and that mammalian data on reprodution, which are more relevant to humans than are *Drosophila* data, do not show a pattern or trend indicative of adverse reproductive effects (51 FR 13376 at 13386). Therefore, the agency found that this observation of fewer offspring in fruit flies fed radiation-sterilized chicken meat was not relevant to the determination of the safety of foods irradiated in compliance with the omnibus regulation.

HEI stated that:

"The Final Report on the Evaluation of the Mutagenicity of Irradiated Sterilized Chicken by the Sex-linked Recessive Lethal Test in *Drosophila melanogaster*" by Raltech Scientific Services revealed that fruit flies fed gamma irradiated checken had seven times fewer offspring than those fed heat treated chicken (See Exhibit D). Efforts to enrich the basal food medium did not affect this finding, and further details of this study would be provided at a public hearing. While the FDA chose to consider this finding an "unreliable indicator of an adverse reproductive effect" (51 FR 13386), other scientists consider the findings alarming and would provide testimony to that effect at a public hearing. The FDA urged that studies on mammals would be more appropriate for reproduction information, but the planned two year Raltech study on rats to look for multigenerational effects was aborted after only 39 weeks, and its results are therefore not adequate to declare safety. (HEI Para. I.19.)

On February 2, 1987, the agency asked HEI to set forth in detail the factual information and analysis that it intended to present in support of this objection at a hearing. HEI submitted a reply on March 6, 1987. Only one of the points that HEI made in its March 6 reply was related in any way to its original objection. In addition to amplifying its original objection regarding the reproductive effects noted in the Raltech *Drosophila* study, HEI referred to the following: a Raltech study of mice fed radiation-sterilized chicken; a Raltech study of rats fed radiation-sterilized chicken; promised testimony by a genetics expert; a study of DNA metabolism in spleen cells of Chinese hamsters fed irradiated fish; and a study of mutation in *Drosophila* fed X-irradiated DNA. FDA has considered all of the points that HEI made in its submissions and, for the reasons considered below, finds that none provide any evidence or rationale that could show that radiation sterilization of chicken caused adverse reproductive effects in *Drosophila*. Neither have they shown why these studies should be considered relevant to the safety of foods irradiated under the conditions of this rule. Thus, in this objection HEI has failed to raise an issue of fact that would justify a hearing (21 CFR 12.24(b)(1)). For the sake of clarity, the agency will discuss each of the points in turn, starting with the Raltech *Drosophila* study.

1. Raltech studies

a. *Raltech Drosophila study.* In its March 6, 1987, response, HEI stated that:

Dr. Thayer reported "* * * an unexplained significant reduction in the production of offspring in cultures of *D. melanogaster* reared on gamma irradiated chicken. This response was dose related and was not overcome by the addition of vitamin supplements." In fact, the table already submitted (which was not part of the Thayer report) demonstrates that the fruit flies fed gamma irradiated chicken have *seven* times fewer offspring than those fed thermally processed (cooked) chicken. A dose response pattern occurred with higher concentrations of gamma-irradiated chicken producing fewer offspring.

Food irradiation proponents declared the results irrevelant, since fruit flies don't normally eat chicken. The table clearly shows that fruit flies consuming no chicken had far more offspring, but it is certainly fair to compare the groups eating the chicken diets or the study would not have been funded in the first place. The positive control, the chicken diet with a known hazardous chemical, led to better reproduction than either the electron or gamma irradiated diets. The fruit flies eating electron irradiated chicken had about three times more offspring than those fed gamma treated chicken, but far fewer offspring than those eating heat treated chicken. (HEI March 6, 1987, response, p. 10 (Ref. 2).)

To justify a hearing, HEI would have to proffer evidence to support its allegation that the *Drosophila* sex-linked recessive lethal mutagenic study with radiation-sterilized chicken meat is relevant for evaluating reproduction effects in mammals, specifically, humans, from foods permitted to be irradiated under FDA's regulation. It has failed to proffer any such evidence.

The sex-linked recessive lethal test in *Drosophila melanogaster* is a standard test designed to detect a particular mutagenic effect, namely, a preferential decrease in male offspring (e.g., see EPA's Toxic Substances Control Act Test. Guidelines, 50 FR 39252 at 39441; September 27, 1985). The study done by Raltech (Ref. 38) with radiation-sterilized chicken did not show this sex-linked recessive mutagenic effect.

Although there was no mutagenic effect observed in this test, the authors noted that *Drosophila* raised on chicken meat had substantially fewer offspring, compared to controls, with the fewest offspring from the *Drosophila* raised on gamma irradiated chicken. As stated above, FDA in its omnibus final rule discounted the significance of this finding on the grounds that the Raltech *Drosophila* study was an unreliable indicator of adverse reproductive effects (51 FR 13376 at 13386).

While, as stated above, FDA has the ultimate burden of proof when it approves the use of a food additive, once the agency makes a finding of safety in a listing document, the burden shifts to an objector to come forward with evidence that calls into question FDA's conclusion. *American Cyanamid Co.* v. *FDA*, supra, 606 F. 2d at 1314–1315. To justify a hearing on this determination, HEI would have to proffer some evidence that demonstrates the relevance of the finding to the safety of food irradiated under the conditions permitted by the omnibus rule or to provide some basis for challenging the reasons that FDA gave for discounting this finding. HEI has failed to do so. It has merely reasserted that there was a finding of reduced offspring.

Significantly, a second study with frozen chicken and gamma irradiated chicken showed that this effect was seen with both types of chicken and was directly related to the amount of chicken meat in the diet (Ref. 38). Based on these results, the agency concluded in the omnibus rule that the observed effect on reproduction could be caused by a number of factors other than irradiation (51 FR 13376 at 13386). HEI has not proffered any evidence that would contradict this conclusion and that would tie this effect directly to irradiation.

Furthermore, as the agency pointed out in the omnibus rule, this test with *Drosophila* has not been designed or validated for testing reproductive toxicity. Reproductive tests are designed to provide information concerning the effects of a test substance on gonadal function, conception, parturition, lactation, weaning and the development of offspring and are therefore carried out in mammalian species (Ref. 39 and, for example, see 50 FR 39252 at 39432). An observation from a study not designed or controlled to test for reproductive effects cannot be used in place of a study so designed and controlled, although it can raise questions for resolution in mammalin reproductive toxicity studies. As stated in the omnibus rule (51 FR 13376 at 13386), mammalian data on reproduction have shown no consistent patterns or trends indicative of adverse reproductive effects from irradiated foods.

Nor has HEI proffered any explanation as to why a study on radiation-sterilized chicken is relevant to the safety of foods irradiated under the conditions permitted by this rule. Rather, HEI has merely asserted that "other scientists consider this finding [of reduced offspring] alarming" and promised to provide testimony at a hearing. A hearing cannot be granted on a mere statement that someone will testify about the relevance of the study without a proffer as to what that person will testify to that demonstrates that there is a genuine and substantial issue of fact that provides a basis for a hearing. *Costle* v. *Pacific Legal Foundation,* supra, 445 U.S. at 214. Thus, HEI has failed to justify a hearing on this issue (21 CFR 12.24(b)(2)).

b. *Raltech mouse study.* In its response, HEI also referred to an increased number of deaths among mice fed gamma-irradiated chicken.

> In studies of mice fed test diets before birth to death or scheduled termination, survival of both sexes was significantly reduced for those fed gamma irradiated food, and the group eating gamma irradiated chicken had the highest incidence of several tumors among those analyzed. To counter claims of possible harm, the National Toxicology Program assembled a new panel to review the slides on lesions in the test animals, and this panel declared that the lesions were not cancerous. Nonetheless, this panel failed to explain the increased number of deaths among the animals eating gamma irradiated chicken. It did demonstrate disagreement among experts. (HEI March 6, 1987, response, p. 10 (Ref. 2).)

Again, HEI has not proffered evidence or explained why this study (Ref. 40), in which radiation-sterilized chicken (irradiated at a dose of 56 kGy) was fed to the mice, is relevant to a rule that does not permit radiation sterilization of chicken. Furthermore, HEI has not proffered any evidence to support its contention that survival was significantly decreased in both sexes. The agency noted a marginally decreased survival in the female mice of the group fed gamma-irradiated chicken but not in the male mice (51 FR 13376 at 13386). Because the decreased survival reported was marginal and occurred only in one sex group, the agency did not consider it to be treatment-related. HEI has not proffered evidence to support its allegation or to challenge the agency's conclusion or to demonstrate why the study should even be considered in this proceeding. In the absence of such a proffer from HEI, there is no basis to find that a meaningful hearing can be held on HEI's claim. (See *Pineapple Growers Ass'n* v. *FDA,* supra, 673 F.2d at 1085.)

HEI also alleges that mice fed gamma-irradiated chicken meat had the highest incidence of "several tumors" but does not specify any tumor type and does not provide any evidence to show that any specific tumor is treatment-related. A hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (21 CFR 12.24(b)(2)). Because HEI has failed to make any proffer in support of its assertion, FDA may properly disregard it. *General Motors Corp.* v. *FERC,* supra, 798 n.20 (D.C. Cir. 1981). Thus, HEI has failed to justify a hearing on this issue.

The agency's review of this study raised concern about the possible treatment-related incidence of only one tumor type, testicular tumors. As discussed in the irradiated pork rule and in the omnibus rule, after examining the histopathology slides, agency scientists concluded that the evidence did not support a treatment-related induction of testicular tumors (50 FR at 29658; 51 FR 13376 at 13386).

Moreover, as noted by HEI, the National Toxicology Program's Board of Scientific Counselors also concluded that the data on testicular tumors do not demonstrate a carcinogenic response. The agency agreed with that conclusion. HEI has not proffered any evidence to challenge the agency's analysis and conclusion (51 FR 13376 at 13386).

c. *Raltech rat study.* HEI stated that a rat study that was not completed should be repeated.

> * * * Although Dr. Thayer did not highlight the problem, one study to explore offspring effects had to be terminated prematurely due to excessive mortality among pups in all diet groups. The study, intended to last two years, was cancelled after only 9 months. Instead of repeating the study to determine the true long-term reproductive effects, the researchers declared the process safe on their limited 9 month data. Critics charge this is a violation of good scientific practice. (HEI March 6, 1987, response, p. 10 (Ref. 2).)

HEI has not proffered any evidence or explained why a study on rats fed radiation-sterilized chicken is necessary to reach a conclusion about the validity of a rule that does not authorize the radiation sterilization of chicken. Nor has it provided any evidence showing that the study raises a health issue about an irradiated food. A hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (21 CFR 12.24(b)(2)). Because HEI has failed to make any proffer in support of its assertion FDA may not properly disregard this study. *General Motors Corp.* v. *FERC,* supra, 798 n.20 (D.C. Cir. 1981). Thus, HEI has failed to justify a hearing on this issue.

The rat study cited by HEI was terminated due to lactation failure in the parent females. This effect was present across all diet groups (i.e., irradiated and control), with no evidence of toxicity due to the test diets (Ref. 41). In order to justify a hearing on this question, HEI must point to evidence either that the terminated study raises a safety issue that challenges the agency's conclusion that food irradiated under the conditions of the omnibus rule is safe, or that such a study is necessary to reach such a conclusion.

Because HEI has not proffered any evidence to support its contention that the absence of a rat reproduction study with radiation-sterilized chicken raises a question on the safety of food irradiated under the conditions of the regulation, it has failed to meet a threshold burden of tendering evidence that suggests there is a need for a hearing on this issue. (See *Costle* v. *Pacific Legal Foundation,* supra, 445 U.S. 214–215, 21 CFR 12.24(b)(2).)

d. *Testimony by a genetics expert.* HEI promised to provide testimony by a

genetics expert regarding the Raltech studies:

Genetic experts like Dr. Cecil B. Jacobson, Director of the Reproductive Genetics Center, will be asked to comment on the relevance of the Raltech findings, which he considered important. (HEI March 6, 1987, response, p. 11 (Ref. 2).)

Announcement of a proposed witness is not a basis for justifying a hearing. HEI has stated that it would ask for testimony from someone like Dr. Jacobson. The mere assertion that an individual may testify on the Raltech findings, without any indication as to what he will testify to, does not provide a sufficient basis on which to grant a hearing. The person seeking a hearing must meet a threshold burden of tendering evidence that suggests the need for a hearing. *Costle* v. *Pacific Legal Foundation,* supra, 445 U.S. at 214. HEI has failed to do so. Thus, it has not established that a factual issue that would justify a hearing exists.

2. Other studies

HEI cited two other studies: a study that reported an effect on DNA metabolism in spleen cells of Chinese hamsters fed irradiated fish (Ref. 29) and a study that reported mutation in *Drosophila* fed x-irradiated DNA (Ref. 42). HEI said of these studies:

Renner, et al., "An Investigation of the Genetic Toxicology of Irradiated Foodstuffs Using Short-term Test System. III—*In Vivo* Tests in Small Rodents and in *Drosophila Melanogaster,*" 20 FOOD CHEM. TOXIC. 867 (1982). This study found that feeding irradiated fish affected DNA metabolism in the spleen cells of Chinese hamsters. Although not cited in the author's summary, Table 6 indicates a significantly different distribution of chromosome number from the control group and the group given unirradiated chicken for number of cells with a chromosome number (2N) 22 at p. 873. This finding should also be considered in regard to Item 18, above.

(HEI March 6, 1987, response, p. 11 (Ref. 2).)

Parkash, O., "Induction of Sex-linked Recessive Lethals and Visible Mutations by Feeding X-Irradiated DNA to Drosophila Melanogaster," 205 NATURE 312 (Jan. 16, 1965). This study quotes Muller as asserting, "It is hardly conceivable that the variety of types of visible mutations could be induced *en masse* by any agent without there being some appreciable effect on the lethal mutation frequency also". Their study fed irradiated DNA to fruit flies and detected a mutagenic effect. The authors state at p. 313, "Further, if our conclusions are substantiated, one might infer that the sterilization of food by using high doses of ionizing radiations is not desirable".

(HEI March 6, 1987, response, p. 11 (Ref. 2).)

The Renner and Parkash studies have nothing to do with the effect of irradiated food on the number of offspring and thus provide no evidence to support HEI's assertion that the reduced number of offspring in *Drosophila* fed radiation-sterilized chicken was caused by irradiation. Renner et al., reported that six in vivo genetic toxicity tests (including a study on DNA metabolism in spleen cells) were carried out on hamsters fed irradiated or nonirradiated cooked chicken, dried dates, and cooked fish (Ref. 29). The agency had reviewed preliminary reports of some of these tests and referenced them in the omnibus rule (51 FR 13376 at 13397) and in the administrative file (81N–0004). The authors concluded that none of the tests provided any evidence of genetic toxicity induced by irradiation. Thus, this study does not provide any basis on which to question the safety of food irradiation.

Table 6, cited in HEI's objections, enumerates the number of cells with chromosomal aberrations in each of the experimental groups. It is true that, in Table 6, the authors reported a difference in the proportion of cells with the normal number of chromosomes in the different treatment groups. However, the proportion of cells with the *normal* number of chromosomes was greater in the hamsters fed irradiated fish than in those fed the control diet (emphasis added). HEI has not explained how a greater proportion of normal cells and a corresponding lesser proportion of abnormal cells in the hamsters fed irradiated fish provides a basis for concluding that ingestion of irradiated foods leads to any adverse effects. Thus, HEI has not justified a hearing on the basis of the Renner study.[3]

Parkash, in a preliminary study, reported a sex-linked recessive lethal effect when fruit flies were fed irradiated DNA (Ref. 42). As discussed earlier, a sex-linked recessive lethal study is designed as an indicator of mutagenicity. HEI has not provided evidence to show how this mutagenicity study can be used to support its claim that irradiated food causes adverse effects on fertility.

Under FDA's regulations, a hearing will not be granted on the basis of mere allegations (21 CFR 12.24(b)(2)). Consistent with this regulation, the relevant case law provides that where a party requesting a hearing only offers allegations without an adequate proffer to support them, the agency may properly disregard those allegations. *General Motors Corp.* v. *FERC,* 656 F.2d 791, 798 n. 20 (D.C. Cir. 1981). In the absence of an explanation of how the Parkash study relates to the alleged adverse effects on fertility in the Raltech study, there is no basis for a hearing on this aspect of the objection.

In addition, Parkash stated that "if our conclusions are substantiated, one might infer that the sterilization of food by using high doses of radiations is not desirable." However, the mutagenic effect reported by Parkash could not be reproduced in later studies (Refs. 43 and 44) designed to test the effect of irradiated DNA on *Drosophila.* These studies, along with the agency's evaluation of the studies, were included in the administrative record of the omnibus rulemaking (see Refs. 3 and 4 in the omnibus rule; 51 FR 13376 at 13397). To justify a hearing on the basis of the Parkash study, HEI would have to provide some basis to find that the Parkash study could be relied on in the face of Parkash's own statement and of the findings in the studies reported in Refs. 43 and 44. HEI failed to do so. Thus, HEI has failed to justify the factual determination its objection urged and thus has failed to justify a hearing on the Parkash study under 21 CFR 12.24(b)(3).

I. Dominant Lethal Tests

HRG objected to the irradiated pork rule and requested a hearing based on a possible risk of chromosome damage. HRG stated that:

A number of studies also raise the possibility that consumption of irradiated food may damage the chromosomes. Such effects have been shown in dominant lethal tests on rats and mice.

In reviewing these and other studies, Dr. Jonathan Ward, of the University of Texas Medical Branch, and an expert in genetic toxicology, concluded that "these studies as a group fail to either prove or disprove the existence of a hazard from the use of irradiated food. It appears possible that unstable mutagenic products may be produced in foods by irradiation * * *. It is difficult to believe that adquate tests of the effects on radiation of food can be conducted without individually evaluating the

[3] Moreover, HEI states that this effect should be considered in regard to Item 18 of their objection (see the earlier discussion on polyploidy). Table 6 demonstrates that there were no increased chromosomal aberrations or polyploid cells in the bone marrow cells of Chinese hamsters given diets of irradiated or unirradiated chicken, dates, or fish for 6 days, and that the number of cells with the *normal* number of chromosomes was higher in the hamsters fed irradiated fish than in those fed untreated fish or the control diet (emphasis added). This evidence contradicts HEI's contention that irradiated food fed to animals results in polyploid cells in the bone marrow cells. HEI has not provided any explanation as to how this evidence can be considered to support its claim.

components of the foods for which radiation sterilization is intended."

(HRG objection, p. 3 (Ref. 37).)

To justify a hearing, a challenge to an agency's factual conclusion must present a live controversy. *Community Nutrition Institute* v. *Young, supra,* 773 F.2d at 1364. In addition, the objection must raise a material issue on which a meaningful hearing might be held. *Pineapple Growers Ass'n* v. *FDA, supra,* 673 F.2d at 1085. HRG's objection fails to meet these requirements.

HRG's objection to the irradiated pork rule quotes a letter from Dr. J. Ward to the Commissioner of FDA. FDA dealt with this letter as a comment in the omnibus rulemaking. At the time of HRG's objection, FDA had not fully considered this comment. Ultimately, FDA responded to this comment in the final rule in the omnibus proceeding (51 FR 13376 at 13385 and 13387), stating that two of the three studies that reported dominant lethal effects were unreliable, and that there was no biological significance to the reported adverse effects in the third study because the results could not be reproduced in three comparable studies. The burden then shifted to HRG to maintain the viability of its objection by proffering some information that called into question the agency's conclusion on this matter. However, HRG failed to object to that conclusion.

As a result, there is no reason to hold a hearing on this objection because there is no live controversy and thus no material issue on which a hearing could be held. In the absence of some explanation from HRG for why the dominant lethal studies showed that irradiation of the food caused the reported effect, in spite of the agency's determination to the contrary in the omnibus rule, it is undisputed that those reports do not provide an appropriate basis on which to question the safety of pork irradiated in accordance with the irradiated pork regulation. Therefore, HRG's objection would not justify the factual determination urged, and FDA is denying HRG's request for a hearing on this issue under 21 CFR 12.24(b)(3).

Moreover, the agency notes that even Dr. Ward's letter does not state that these studies demonstrate that irradiated food caused dominant lethal mutations. Dr. Ward stated only that "these studies as a group fail to either prove or disprove the existence of a hazard from the use of irradiated food * * *. I would encourage the FDA to carefully evaluate the existing data" (Ref. 45). The agency did not base its decision on safety solely on these studies but did carefully evaluate all available toxicology data (51 FR 13376 at 13378). Therefore, there is no dispute with the letter cited by HRG in its objection.

J. In Vitro Effects of Irradiated Sugar Solutions

In the omnibus rule, the agency responded to a comment that sugars irradiated in simple solution have been shown to cause toxic biological effects during in vitro testing (51 FR 13376 at 13383). The agency agreed that such effects were seen with simple sugar solutions but cited reports that found that irradiation of sugars in food, that is, in typically complex food matrices, does not produce the same toxic effect that occurs when these sugars are irradiated in simple solution. The agency stated:

> There is ample evidence that the types and quantities of radiolytic products from irradiation of sugar solutions are not only dose dependent but are also dependent on specific conditions such as oxygen concentration and metal ions present in foods but not present in simple sugar solutions.

(51 FR 13376 at 13383.)

The agency concluded that "* * * irradiated aqueous sugar solutions are unsuitable models for predicting and extrapolating toxicity of irradiated foods * * *. Additionally, no evidence indicates that irradiated foods, including those containing sugars, will cause adverse toxic effects to animals or humans."

(51 FR 13376 at 13383.)

HEI's objection stated:

> The FDA admitted that "irradiated solutions of sugars have been shown to cause biological effects in vitro" (51 FR 13383), but argued that the adverse findings would not apply to complex food matrices. Evidence of the applicability of these findings to fruits and vegetables would be offered at a public hearing.

(HEI Para. I.17.)

On February 2, 1987, the agency asked HEI to set forth in detail the factual information and analysis that it intended to present at a hearing. On March 6, 1987, HEI responded by citing a 1982 study by Adam on radiolysis of *alpha, alpha*-trehalose in concentrated aqueous solution (Ref. 46); two in vitro mutagenic studies, one conducted by Holsten et al. (Ref. 47) on the effect of irradiated sugar solutions on carrot tissue cultures and the other by Shaw and Hayes (Ref. 48) on the effect of irradiated sugar solutions on leucocyte cell cultures; and two chapters on radiation chemistry of foods, one by Basson (Ref. 49) and the other by Beyers et al. (Ref. 50), from a 1983 book, "Recent Advances in Food Irradiation."

A hearing will not be granted on the basis of mere allegations or general descriptions and contentions (21 CFR 12.24(b)(2)). HEI must, at a minimum, "raise a material issue concerning which a meaningful hearing might be held." *Pineapple Growers Ass'n of Hawaii* v. *FDA,* supra, 673 F.2d 1085.

As stated earlier, FDA does not dispute that irradiated sugar solutions have caused toxic effects in cell cultures. However, the agency concluded in the omnibus rule that irradiated sugar solutions are unsuitable models for predicting toxicity of irradiated foods (51 FR 13376 at 13383). The first article cited by HEI (Ref. 46) reports on experiments showing that common food components mixed with sugar solutions can affect the final composition of radiolytic products formed from the sugar, consistent with FDA's conclusion that the types and quantities of radiolytic products depend on specific conditions present in foods but not present in simple sugar solutions (51 FR 13376 at 13383). The other two articles (Refs. 47 and 48) merely report the results of in vitro tests with simple sugar solutions.

HEI has not provided any evidence or rationale for concluding that in vitro toxicity studies using simple sugar solutions are suitable models for evaluating the safety of eating foods, such as fruits and vegetables, irradiated under the conditions of the regulation. To justify a hearing, HEI must provide some basis on which to find that FDA's conclusion on the relevance of these studies was incorrect. It has failed to do so, however. Thus, the objector has not met its "threshold burden of tendering evidence suggesting the need for a hearing." (See *Costle* v. *Pacific Legal Foundation,* supra.)

Moreover, the authors of the chapters (Refs. 49 and 50) cited by HEI concluded that radiolysis products from carbohydrates, including simple sugars, are not a hazard (Ref. 49, p. 23), and that in vitro studies with simple sugars are not applicable to the safety of irradiated fruits and vegetables (Ref. 50, p. 176). This conclusion is consistent with the agency's analysis, and these chapters were referenced by FDA in its final rule (51 FR 13376 at 13379 and 13383).

HEI cites selected parts of these chapters out of context to reach a conclusion that is opposite to that of the authors. HEI stated that:

> This study [by Basson] states, "* * * the chemical changes following irradiation of a model fruit cell are dominated by the radiolytic decomposition of the sugar fraction" at page 12. It notes at page 13, "The radiolysis of oxygen in dilute aqueous solutions leads almost exclusively to the production of hydrogen peroxide," which is

"mildly cytotoxic * * *." Rapid destruction of hydrogen peroxide is claimed for fruits, but that is not the same as total destruction of possible hazardous molecules. The importance of sugar exposure to radiation should be apparent from the statement at page 12, "The maximum yields of all radiolytic products due to an individual component have been calculated and it is clear how the carbohydrates (glucose, sucrose, fructose) contribute overwhelmingly to the product spectrum." Given the importance of sugars in the average daily diet, radiation effects on sugars cannot be "assumed" to be safe.

(HEI March 6, 1987, response, p. 7 (Ref. 2).)

HEI, however, eliminates the conclusions reached by the author. Basson stated:

No consistent mutagenic activity due to these products could be shown using the Ames test and none was observed in a host-mediated assay. Furthermore, it was shown that the presence of other fruit components eliminated any genotoxic activity and this is consistent with the observation that real fruits do not develop genotoxic activity in test systems as a result of irradiation.

The radiolysis of oxygen in dilute aqueous solutions leads almost exclusively to the production of hydrogen peroxide. In these model systems, hydrogen peroxide has been shown to react readily with a number of food components such as enzymes, trace metals and certain amino acids. Thus although hydrogen peroxide is mildly cytotoxic it does not present a hazard when produced in the presence of typical fruit components because of its rapid destruction.

(Ref. 49, p. 12.)

Thus, Basson's discussion explains why in vitro studies of irradiated sucrose solutions are not good models for irradiated fruits. The agency agreed with Basson's analysis in the omnibus rule (51 FR 13376 at 13383). HEI has proffered no evidence for challenging this conclusion. Thus, the Basson chapter, rather that justifying resolution of the issue of the significance of in vitro studies of irradiated sugar solutions in the way sought by HEI, supports exactly the opposite conclusion. (See 21 CFR 12.24(b)(3).)

HEI cites the chapter by Beyers et al.:

This paper summarizes research that the FDA should carefully scrutinize. While the authors of this study conclude that irradiation is no more destructive to food than heating, the destruction caused by irradiation will often be added to heating in cooking preparation of food.

The Beyers study cites evidence of harmful effects of ionizing radiation, such as mutagenicity studies carried out on various irradiated sugar solutions cited at page 175. The spot test and the Ames test were used to detect mutagenic effects of irradiated sugar solutions and radiolytic products of the sugars. The results were positive for sugar solutions in four cases for the spot test and in three cases for the Ames test. The host-mediated assay was negative for all four. We do not believe that one should dismiss the adverse findings and rely only on the tests which showed no mutagenicity. The Beyers new work found all five irradiated sugars studied to be mutagenic in at least one instance and found the presence of oxygen had a marked influence on the mutagenic response of irradiated sugar solutions. The authors concluded that the interaction of these sugars with other components of actual fruits could account for the absence of mutagenic response in animal feeding studies, but we contend that the danger of irradiated sugars needs further study.

(HEI March 6 response, p. 7 (Ref. 2).)

HEI's contention "that the danger of irradiated sugars needs further study" adds nothing to the discussion above. HEI states that the chapter summarizes research that FDA should scrutinize but then disagrees with the authors' analysis, without providing any evidence to support its disagreement, and ignores the authors' cautionary advice on misinterpretation of data. In this article the authors state:

To assess the relevance of the observed mutagenic effects on the safety of irradiated foods, experiments were carried out on mammalian cells (Swiss albino male mice). None of the four tester strains which had shown biological activity in the *in vitro* experiments showed any evidence of an increased reversion frequency. It was pointed out that extrapolation of findings with cell cultures and simple forms of life to the more complex mammalian systems should be carried out with great caution as they may be meaningless.

(Ref. 50, p. 176.)

Scrutiny of the evidence that HEI has referenced reveals that that evidence does not challenge FDA's conclusion that the in vitro studies are not applicable to the safety of fruits and vegetables irradiated under the conditions of the regulation.

Thus, HEI's objection, when fully analyzed, consists of its unsupported allegation that the results of in vitro testing of irradiated sugars are applicable to complex food matrices. As stated earlier, a bare contention without facts cannot be a basis for a hearing. Because HEI has not proffered any evidence that supports its general contention, it has failed to meet a threshold burden of tendering evidence that suggests there is a need for a hearing on this issue (See *Costle* v. *Pacific Legal Foundation, supra*) (21 CFR 12.24(b)(2).)

K. Effect on Pathogenic Microorganisms

In the omnibus rule, the agency addressed comments that asserted that irradiation intended to eliminate one food hazard may affect the microbial spoilage patterns of foods, thereby creating a new food hazard. These comments expressed concern that *Clostridium botulinum* spores would survive irradiation and would produce botulin toxin without typical signs of food spoilage. The agency concluded that this concern did not apply to the uses of irradiation permitted under the regulation because dry foods (such as spices) do not provide a growth medium for *C. botulinum* spores, and a 1 kGy radiation dose is too low to change normal spoilage patterns (51 FR 13376 at 13381).

1. Change in spoilage patterns

HEI stated that:

FDA admits that irradiation intended to eliminate one food hazard may affect the microbial spoilage patterns of food, thereby creating a new hazard, especially the *C. botulinum* spores (51 FR 13361) [sic]. The FDA argues that this concern does not apply to irradiation of dry foods or foods treated below 100,000 rad. FDA has not addressed the issue of botulism in wet foods, such as canned tomatoes or other wet foods approved for irradiation under this rule. The FDA regulation would continue to allow irradiation of fresh pork below 100,000 rads, and botulism organisms that might be present on fresh pork will not be destroyed by 100,000 rads of radiation. However, in an April 7, 1986 letter to Martin A. Welt, FSIS Deputy Administrator Dr. Ronald E. Engel warned: "After careful review of the scientific literature by our scientists, outside consultants, and the FDA (Food and Drug Administration), it was concluded that there are no data to support the microbiological safety of irradiated vacuum-packaged pork at an absorbed dose of 30–100 kilorad. Further, we believe that any initiative to sell and distribute perishable irradiated products through the mail or through methods other than the usual commercial distribution channels should not be permitted * * *. *When a vacuum-packaged fresh pork product has been irradiated between 30–100 kilorad there is a concern that a potential health hazard might result from further reducing the natural flora and allowing Clostridium botulinum spores, if present, to produce toxin under conditions where typical spoilage is not evident.*" (emphasis added [by HEI]).

The FDA has clearly failed to properly address this important concern, and further evidence will be offered at a public hearing.

(HEI Para. I.13.)

A hearing will not be granted on the basis of mere allegations or general descriptions and contentions (21 CFR 12.24(b)(2)). HEI alleges that the agency had not addressed the issue of botulism in "wet" foods.[4] FDA's conclusion in the

[4] The agency assumes that HEI's use of the term "wet" foods was to distinguish "dry" foods, such as spices, from all other foods that contain significant amounts of water.

final rule that irradiation of food below 1 kGy will destroy few spoilage bacteria and thus will not change normal spoilage patterns applied to all food, including "wet" foods (51 FR 13376 at 13381). Thus, FDA did address this issue.

While, as stated above, FDA has the ultimate burden of proof when it approves the use of a food additive, once the agency makes a finding of safety in a listing document, the burden shifts to an objector to come forward with evidence that calls into question FDA's conclusion. *American Cyanamid Co.* v. *FDA, supra,* 606 F.2d at 1314–1315. HEI has not presented any evidence to demonstrate that irradiation of "wet" foods under the conditions permitted would affect the common spoilage pattern enough to create a new microbial hazard with botulism. In the absence of such evidence, HEI has provided no basis to justify a hearing.

Moreover, HEI's reference to botulism in canned tomatoes demonstrates a lack of understanding about what is permitted under this regulation and about food processing practices. Fresh tomatoes may be irradiated at low doses to control insects or to inhibit ripening, but such extra processing would not normally be done for a product to be thermally processed nor for a canned product. More important, any effect of precanning radiation processing on spoilage organisms or *C. botulinum* spores, even at doses permitted by this regulation, would be superseded by the total sterilization of the food during the canning process.

HEI's objection was filed to the omnibus rule, which did not pertain to the irradiation of pork. Irradiation of pork was permitted under the rule issued on July 22, 1985 (50 FR 29658). HEI's objection was submitted nearly 9 months after publication of the irradiated pork rule in the **Federal Register,** long after the 30-day objection period. Therefore, HEI's objection with respect to pork is not timely. *ICMAD* v. *HEW,* 574 F.2d 553, 558 n.8 (D.C. Cir.), *cert. denied* 39 U.S. 893 (1978).

Moreover, HEI's statement that "[t]he FDA regulation would continue to allow irradiation of fresh pork below 100,000 rads, and botulism organisms that might be present on fresh pork will not be destroyed by 100,000 rads of radiation" is not an issue in dispute. HEI has not presented any evidence to show that irradiation of pork under these conditions will affect the common spoilage pattern enough to create a new microbial hazard with botulism. Therefore, under 21 CFR 12.24(b)(2), HEI has failed to justify a hearing with this allegation.

The USDA letter cited by HEI deals only with the vacuum packaging of low dose irradiated pork and shipment of such pork through the mail. As noted in the letter, vacuum packaging of irradiated pork is not permitted by USDA. (USDA has jurisidiction over meat products under the Federal Meat Inspection Act (21 U.S.C. 601 *et seq.*).) A hearing will not be granted on factual issues that are not determinative with respect to the action requested (21 CFR 12.24(b)(4)). Vacuum packaging of pork is not an issue in these final rules and thus not a basis for granting a hearing.

As for HEI's claim that it would produce further evidence at a hearing, as stated above, a hearing cannot be justified on the basis of a promise that some unidentified evidence will be provided at the time of that hearing. The person seeking a hearing must meet a threshold burden of tendering evidence that suggests the need for a hearing. *Costle* v. *Pacific Legal Foundation, supra,* 445 U.S. at 214. Thus, HEI has not proffered any evidence relevant to its contention that irradiation of food under the conditions of this regulation would create a new microbiological hazard.

2. Mutation of microorganisms

In adopting the omnibus rule, FDA considered comments that irradiation may create or produce potentially harmful radiation-resistant bacteria, new bacteria, or viral mutants. The agency concluded that the possibility was remote that organisms affected by mutatiions would be more virulent ormore harmful than those created in nature (51 FR 13376 at 13382).

HEI stated that:

> The FDA dismissed the problem of the creation of mutant bacteria and viruses by suggesting that mutations do occur naturally, and the increased mutations caused by ionizing radiation should therefore be ignored or discounted (51 FR 13361) [sic]. Diseases such as AIDS may well be the product of mutant viruses, and public health authorities would certainly agree that steps to prevent the spread of such viruses are essential to maintaining public health. Yet the FDA, without specific scientific evidence to support it, argues that mutant viruses or bacteria cannot be more harmful than those occurring naturally. The FDA further argues that if a hazard might exist naturally, the FDA has no obligation to prevent the increase of such a hazard. This attitude is clearly in violation of the Federal Food, Drug and Cosmetics [sic] Act. The proposed doses of irradiation are clearly doses that will allow bacteria and viruses to survive on foods, since very high doses (generally in the millions of rads) are needed to kill them. Ionizing radiation is a well established mutagenic agent, and the FDA response to comments warning of this danger is simply speculative and inadequate. Further evidence by appropriate scientists and professionals will be offered at the public hearing.

(HEI Para. I.14.)

A party requesting an evidentiary hearing cannot rely merely on speculation to support its request. To justify a hearing on this objection, HEI must offer some evidence that supports its contention that dangerous mutant viruses or bacteria will be created by irradiation of food at the levels permitted by FDA. For example, this standard could have been met if HEI had submitted evidence on the types of mutant viruses and bacteria found in irradiated foods, evidence on the conditions that exist during irradiation that make it likely that mutations affecting safety will occur, or some other evidence that would provide a basis to call into question FDA's conclusion that the possibility that harmful mutant organisms will be produced is remote. Yet, HEI has not made any such proffer. HEI has provided no evidence to support its allegations.

The agency finds that this objection is merely a general description of HEI's position, and that it does not raise a factual issue for resolution at a hearing. Therefore, HEI has failed to justify a hearing under 21 CFR 12.24(b)(2).

HEI's promise to provide unspecified evidence does not remedy this deficiency. A hearing cannot be justified on the basis of a promise that some unidentified evidence will be provided at the time of that hearing. The person seeking a hearing must meet a threshold burden of tendering evidence that supports the need for a hearing. *Costle* v. *Pacific Legal Foundation, supra,* 445 U.S. at 214.

There is no dispute that radiation, like heat, can cause mutations but that does not mean that irradiation of food causes mutations that present new safety problems. In response to a comment in the omnibus rule (51 FR 13376 at 13382), FDA referenced a report of a 1982 meeting of the Board of the International Committee on Food Microbiology and Hygiene of the International Union of Microbiological Societies (Ref. 51). At that meeting, the Board concluded that "Irradiation induced genetic mutation of pathogens in food did not create an increased hazard to health and in the Board's opinion there would be no qualitative difference between the kind of mutation induced by ionizing irradiation and that induced by any other pasteurization/partial preservation methods such as heat treatment or vacuum drying." Other studies have come to the same conclusion (See Refs. 52 to 54).

3. Effect on aflatoxin production

In the omnibus rule (51 FR 13376 at 13381), FDA responded to a comment that cited studies by Priyadarshini and Tulpule in which aflatoxin producing organisms were added to wheat after irradiation and autoclaving (steam sterilization), as well as to wheat that had been autoclaved only. Increased levels of aflatoxin were reported in the wheat that had been irradiated. FDA concluded that the studies did not replicate actual food handling practices in that wheat would not be steam-sterilized in addition to being irradiated, and that infection with aflatoxin producing organisms would ordinarily occur before harvest. FDA noted that it had no evidence that would lead it to conclude that food irradiated and stored under normal handling practices would show increased aflatoxin production and concluded that the results cited did not justify modification of the rule.

In its proposal for the omnibus rule (49 FR 5714 at 5717), FDA cited a report by Schindler that irradiation of mold spores in aqueous suspension may increase aflatoxin production but noted that other studies had shown either no increase or a decrease in aflatoxin production after irradiation. FDA tentatively concluded in the proposal that because this study did not replicate actual use conditions its results were not an adequate basis for concluding that irradiation of food should not be permitted. Comments on the proposal did not address the Schindler study on whether an adequate study must replicate actual use conditions.

HEI objected to the omnibus final rule on the ground that:

> The FDA dismissed evidence that aflatoxin production can be increased by exposure to ionizing radiation, citing two studies by Priyadarshini & Tulpule as being inappropriate because "the studies referenced do not replicate actual food-handling practices" (51 FR 13361) [sic]. Whether a scientific study replicates food handling practices is not the issue here. The issue is whether a greater danger to consumers is created by the increased production of fungal toxins due to irradiation. Aflatoxin production is already a well known problem in terms of our food supply. Since naturally occurring aflatoxin contamination of foods has been identified as a problem in many countries * * *, the FDA ought to be aware of this problem. The FDA earlier cited Schindler, A.F., et al., "Enhanced Aflatoxin Production by *Aspergillus flavus* and *Aspergillus parasiticus* after Gamma Irradiation of the Spore Innoculum [sic].: JOURNAL OF FOOD PROTECTION, 43:7–0, 1980, and Applegate, K.L. and J.R. Chipley, "Increased Aflatoxin Production by *Aspergillus flavus* via Cobalt Irradiation," POULTRY SCIENCE, 52:1492–1496, 1973, which found increased aflatoxin production after irradiation. The above studies compared non-irradiated foods with irradiated foods, and found greater aflatoxin production in the irradiated foods. While all of these studies were conducted in laboratories, where before and after conditions could be properly evaluated, one cannot claim that the aflatoxins will magically disappear from the food environment before foods reach a food irradiator. The scientific literature indicates that the Environmental Protection Agency considers aflatoxins a potent carcinogenic hazard, and therefore, the FDA should either present evidence to refute the scientific studies cited above or prevent its use based upon the greater danger of aflatoxin production on foods so treated. Further evidence regarding the stimulation of aflatoxins would also be offered at a public hearing.

(HEI Para. I.12.)

On March 6, 1987, HEI responded to an FDA request for the evidence that it intended to present on this issue by citing a statement by Horace Graham in a 1980 book (Ref. 55) that more information is needed. HEI also cited: an EPA document that ranked aflatoxin B–1 high in its list of suspected carcinogens; a statement by Dr. Lester Crawford (Associate Administrator of the Food Safety and Inspection Service, USDA) that "if studies show increased aflatoxin production on irradiated foods, he would be concerned, since aflatoxin is considered most carcinogenic;" a book section on aflatoxin toxicity and mechanism of action; and a study on an epidemic of hepatitis in humans who consumed contaminated maize.

Given FDA's conclusion in the final rule that "[t]he agency has no evidence that would lead it to conclude that food irradiated and stored under normal handling practices would show increased aflatoxin production" (51 FR 13376 at 13381), it is not enough for HEI to assert that the issue is not whether the study replicates food handling practices. To justify a hearing, HEI must point to some basis for finding that FDA's conclusion is wrong. HEI must either point to some evidence that the aflatoxin concentration on food under actual food handling conditions would be increased by irradiation or explain why the laboratory studies that FDA stated are not relevant to actual food handling practice should be considered relevant. HEI has failed to do so. Therefore, HEI has failed to justify a hearing.

While, as stated above, FDA has the ultimate burden of proof when it approves the use of a food additive, once the agency makes a finding of safety in a listing document, the burden shifts to an objector to come forward with evidence that calls into question FDA's conclusion. *American Cyanamid Co.* v. *FDA, supra*, 606 F.2d at 1314–1315. HEI has not presented any evidence to challenge FDA's conclusion that foods irradiated and stored under normal handling practices do not show increased aflatoxin production. In the absence of such evidence, HEI has provided no basis to justify a hearing.

FDA does not disagree with HEI's statement in its March 6, 1987, submission that aflatoxin B–1 is a carcinogen; that a significant increase in aflatoxin in the food supply would be of concern; that aflatoxins are toxic; and that aflatoxin consumption has been associated with outbreaks of hepatitis. Furthermore, FDA has never claimed that "aflatoxins will magically disappear from the food environment before foods reach a food irradiator," as stated in HEI's original objection.

None of this information, however, challenges FDA's conclusion that foods irradiated and stored under normal handling practices do not show increased aflatoxin production. Because HEI has failed to challenge FDA's conclusion, it has failed to justify a hearing on that conclusion. A hearing will not be granted if there is no genuine issue of fact for resolution (21 CFR 12.24(b)(1)).

The statement by Graham cited by HEI states that "[m]ore information on the effects of low level irradiation on mycotoxin-producing molds is needed * * *." Graham (Ref. 55) goes on to say that post-irradiation handling of any food, including grains, should be done in such a way as to preclude the outgrowth of toxin-forming, or any other type, of spoilage organism. He stressed the importance of the storage temperatures, the relative humidity of the storage atmosphere, and the water content of the food product. Graham referenced a study by Behere et al. (Ref. 56). This study, which closely resembled actual food handling conditions, showed no radiation-related increase in the amount of toxin produced in grains artificially infected with *A. flavus* before or after irradiation at a dose of 0.2 kGy (Ref. 56). The authors of the study stated that the storage experiments showed that the moisture content of the grain was critical for fungal growth and aflatoxin production. Thus, Behere's study, and hence Graham's chapter cited by HEI, are consistent with FDA's conclusion that foods irradiated and stored under normal handling practices do not show increased aflatoxin production. Consequently, this study does not create an issue of fact and does not provide a basis for a hearing on FDA's conclusion (21 CFR 12.24(b)(1)).

L. Trichinosis

Several objections to the irradiated pork rule stated that there are no significant benefits to food irradiation, and that other methods to control *Trichinella spiralis* exist. In addition, they stated that trichinosis is not a serious health problem and requested a hearing because there are cheaper and safer ways to control trichinosis.

FDA concluded that irradiation of pork at 0.3 to 1 kGy is a safe and effective means of controlling *Trichinella spiralis*. The seriousness of the health hazard from trichinosis or the availability of alternative methods for preventing this health problem are not factors that can be considered under the Food Additives Amendment.[5] Rather, a decision to permit use of an additive must be based solely on consideration of whether it is safe under the conditions of use, and whether it performs the intended technical effect. Thus, even if the objectors could show there are cheaper and safer ways to control trichinosis, such a showing would not provide an appropriate basis for the agency to change its conclusion. Therefore, the objectors did not justify a hearing under 21 CFR 12.24(b)(4).

M. Free Radical Formation

In the final rule, FDA stated that free radicals are formed during irradiation of food and dissipate quickly in the presence of water (51 FR 13376 at 13379). Free radicals formed in dry spices and seasonings are known to persist for long periods of time while these foods remain dry but dissipate quickly when the dry ingredient is added to moist foods (51 FR 13376 at 13379). FDA noted that free radical reactions are also common during conventional food processing. The agency stated that the important question in deciding on the safety of irradiated foods was not whether free radicals may be formed, but whether a toxic radiolytic product could be formed in sufficient amounts to make the food unsafe. FDA concluded that the evidence does not show that toxic radiolytic products are formed in sufficient amounts to cause concern about the safety of irradiated foods (51 FR 13376 at 13378).

HEI objected on the basis that:

> Free radical formation is currently a prime area of investigation of cancer induction, and should not be ignored merely because such substances may be present (and causing cancer) in other foods. FDA's comment that "[because] irradiation produces free radicals as reactive intermediates in the food itself, the high water content of all fresh food provides a medium for their rapid degradation" (51 FR 13379). This statement is erroneous for two reasons. First, this statement clearly contradicts FDA's approval of spice irradiation, which the agency states was "based on the fact that the amount of chemical change in the solid, dry state of a food is less than would occur when substantial portions of liquid are present" (51 FR 13380). Secondly, the issue with free radicals is that they form new chemical bonds of unknown toxicity which are then ingested into the body. FDA's statement that "they are not likely to persist or be present at all in food by the time that food reaches the consumer" (51 FR 13379) is misleading at best, as the dangers of free radicals do not necessarily consist of their reactions *inside the body*, but rather within the food prior to consumption. Since FDA does not know what the long-term health effects of consuming such foods is, it should withdraw its regulation and hold a public hearing to consider evidence as to the adverse effects of such foods.
>
> (HEI Para. I.6 Emphasis added by HEI.)

The agency asked HEI on February 2, 1987, to set forth in detail the factual information and analysis on this objection that it intended to present at a hearing.

On March 6, 1987, the objector: (1) Stated that Dr. George Tritsch would testify on the relationship of free radical formation and cancer, (2) cited three articles discussing free radicals in food, and (3) referred to statements by two persons that more studies should be done. HEI's original objection and supplementary response raise several distinct concerns, none of which present an issue of fact that would justify the granting of a hearing on the safety of food irradiation.

1. Alleged contradiction

In the original objection, HEI stated that "FDA's comment that '[because] irradiation produces free radicals as reactive intermediates in the food itself, the high water content of all fresh food provides a medium for their rapid degradation' (51 FR 13379) * * * is erroneous" because it "contradicts FDA's approval of spice irradiation, which the agency states was 'based on the fact that the amount of chemical change in the solid, dry state of a food is less than would occur when substantial portions of liquid are present' (51 FR 13380)." HEI has not explained why it believes that these statements are contradictory.

HEI's allegation appears to be based on a misunderstanding of free radical chemistry. In foods with high water content, the free radicals that are produced during irradiation degrade quickly to form radiolytic products (51 FR 13376 at 13380). Thus, the free radicals are short-lived and chemical change occurs readily. In dry, solid foods, such free radicals are less able to react to form radiolytic products and therefore persist longer as free radicals (51 FR 13376 at 13380). In general, the amount of radiolytic products formed by irradiation is less in those foods that are dry than in foods with high water content (49 FR 5714 at 5716).

The person seeking a hearing must meet a threshold burden of tendering evidence that suggests the need for a hearing. *Costle* v. *Pacific Legal Foundation*, supra, 445 U.S. at 214. By merely asserting that the statements are contradictory but not submitting any evidence to support that assertion, HEI has failed to demonstrate that an issue of fact exists. Thus, there is no basis for a hearing on this assertion under 21 CFR 12.24(b)(2).

2. Free radicals and cancer research

HEI stated that Geroge Tritsch, Ph.D., a researcher at the Roswell Park Memorial Institute, would summarize scientific investigation into free radical formation and its relation to induction of cancer.

A hearing request must raise a material issue of fact concerning which a meaningful hearing might be held. *Pineapple Growers Ass'n* v. *FDA*, supra, 673 F.2d at 1085. The statement that "free radical formation is currently a prime area of investigation of cancer induction" is not in dispute. Thus, this statement does not justify a hearing under 21 CFR 12.24(b)(1).

Moreover, a hearing cannot be justified on the basis of a promise that some unidentified evidence will be provided at the time of that hearing. To justify a hearing, HEI would have to provide some basis to believe that the investigations to be summarized by Tritsch raise questions about the safety of irradiated foods. The mere assertion that an individual will summarize investigations on the relationship of free radical formation and cancer does not establish that such investigations are relevant to the safety of irradiated foods and therefore justify a hearing. The person seeking a hearing must meet a threshold burden of tendering evidence that suggests the need for a hearing, *Costle* v. *Pacific Legal Foundation*, supra, 445 U.S. at 214, and HEI has not done so with respect to this objection.

[5] The agency still believes, however, that trichinosis is a serious public health hazard and infections can lead to death. Although the incidence of trichinosis has declined in recent years, there are still enough outbreaks from eating insufficiently cooked pork to warrant concern. In fact, there are probably more incidents of trichinosis than of foodborne botulism (Ref. 57). Treatments such as the use of irradiation ensure that pork products are not the sources of trichinella infection.

3. Production of free radicals in food

HEI referred to articles by Basson (Ref. 49), Simic et al. (Ref. 58), and Kesavan (Ref. 59) as evidence that free radical formation occurs in foods exposed to ionizing radiation. HEI stated:

> Basson * * * notes at page 11, "When the model fruit cell is irradiated, nearly all the incident energy is absorbed by the water (80–90% of the cell mass) and leads to the production of water free radicals * * *"
>
> Simic, et al. * * * point out that radiation-induced free radical reactions which occur in irradiated foods are responsible for all the biological and chemical effects, desirable or undesirable, producing a variety of radiolytic products that are dependent on dose, dose rate, temperature, atmosphere, physical state and extent of hydration. We [HEI] believe that the radiolytic products in each food item should be examined on a case by case basis, rather than granting blanket safety approval for all food irradiated at low doses, since such safety cannot rationally be assumed.
>
> * * * Kesavan, discussing irradiation of food, admits, "Dry seeds and food subjected to high doses do contain large amounts of free radicals." Kesavan suggests that since these free radicals dissipate with storage, we should not be concerned. Since FDA does not require storage of irradiated foods until dissolution of free radicals, and since some studies suggest adverse effects from freshly irradiated food (Bhaskaram, discussed later), we disagree.

(HEI March 6, 1987, response, p. 1 (Ref. 2).)

The statements that HEI references do not justify the granting of a hearing. A hearing will not be granted unless there is a genuine and substantial issue of fact for resolution (21 CFR 12.24(b)(1)). FDA does not dispute the statements made by the authors of these references. The agency agrees that free radicals are formed in food during irradiation (51 FR 13376 at 13379).

The first two references that HEI cites are simply examples of many similar reports that discuss radiation chemistry of foods and food components. FDA used these reports to support its finding that products formed during irradiation are predictable.

On the basis of these reports, HEI asserts that radiolytic products in each food item should be examined on a case-by-case basis. Yet, HEI has not cited anything in these two reports that supports this assertion. Neither Basson nor Simic et al., state that food items must be evaluated on an individual basis nor does either author present any evidence that would justify a case-by-case evaluation. Thus, all that HEI has really presented is an unsupported statement of its belief on how safety assessments should be made. A hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (21 CFR 12.24(b)(2)). Because HEI has failed to make any proffer that supports its assertion, FDA may properly disregard it. *General Motors Corp.* v. *FERC*, 656 F. 2d 791, 798 n. 20 (D.C. Cir. 1981). Thus, HEI has failed to justify a hearing on this issue.

HEI, in discussing the Kesavan article, implies that the amount of free radicals in dry foods is a basis for requiring a mandatory storage period, although Kesavan did not reach this conclusion. HEI claims that irradiated foods are unsafe because FDA has not required a minimum storage period.

In the omnibus rule, FDA found that it was not necessary to establish a minimum storage period because there was no evidence that pointed to such a need. To establish that an issue exists, and thus to justify a hearing, HEI would have to point to evidence that shows that FDA erred, and that some minimal storage period is necessary to dissipate free radicals and to assure the safety of irradiated food. *American Cyanamid Co.* v. *FDA*, supra, 606 F. 2d at 1314–1315. HEI has not cited any study in which free radicals in foods were found to cause harm. It references only the Bhaskaram study in support of its claim that adverse effects are associated with freshly irradiated food. As previously discussed, however, FDA considered the Bhaskaram study (See II. D. *Polyploidy* above) and found that it does not provide a valid basis on which to judge the safety of such food. HEI has not cited any other evidence to support its contention here. Therefore, HEI has not provided any basis for concluding that the presence of free radicals in irradiated food requires that a mandatory storage period for that food needs to be established and thus has failed to meet its threshold burden of tendering evidence that suggests the need for a hearing on this issue. *Costle* v. *Pacific Legal Foundation, supra*, 445 U.S. at 214. Thus, HEI has failed to justify a hearing under 21 CFR 12.24(b)(1).

Moreover, a study designed specifically to address whether free radicals that might persist in food pose a serious safety concern has been conducted (cited as reference 34 by FDA in the omnibus rule). In that study, "Long Term Animal Feeding Study for Testing the Wholesomeness of Irradiated Diet with a High Content of Free Radicals" (Refs. 60 and 61), rats were fed a diet containing 35 percent dry milk that was irradiated at 45 kGy shortly before feeding and that still contained a high quantity of free radicals, as measured by electron paramagnetic resonance spectrometry. This use of a very high radiation dose for a large fraction of the diet is far in excess of what is permitted by the omnibus rule. The authors reported no treatment-related toxicological effects from the free radicals present in the milk-powder diet.

4. Need for more studies

HEI referred to a statement on food irradiation by USDA's A.E. Olson at the Second National Conference for Food Protection (1984), and quoted from a 1980 book, *Safety of Foods*, by Graham (Ref. 55). Of Dr. Olson's statement, HEI stated:

> A.E. Olson, of the U.S. Department of Agriculture, recently said in the proceedings of the Second National Conference for Food Protection, May 1984, regarding food irradiation: "As this process becomes important in the preparation of a particular food, studies should be undertaken on the possible formation of toxic compounds in that food and the effects on [sic] the processing on nutrient bioavailability. Particular attention should be directed to the possible formation of any previously unidentified compounds in that food and how they may affect food safety and nutrition."

(HEI March 6, 1987, response, p. 2 (Ref. 2).)

HEI also asserted that Graham's chapter, "Safety and Wholesomeness of Irradiated Foods" (Ref. 55) stated that: "* * * more work needs to be done before convincing conclusions can be arrived at' regarding carcinogenicity of irradiated foods, despite the large number of studies already conducted."

A hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions (21 CFR 12.24(b)(2)). The statements that HEI cites concern food irradiation in general. HEI has failed to show that either of these general statements raises questions about the agency's specific findings on minor dry ingredients and foods irradiated at a low dose. In general, the agency agrees with Olson and Graham that particular attention should be directed to the possible formation of any previously unidentified compounds in irradiated food and to how these compounds may affect food safety and nutrition. In this instance, however, the agency found that the evidence was adequate to conclude that food irradiated under the conditions of the regulation is safe. HEI has not presented any basis to believe that either author would disagree. Thus, in the absence of evidence that ties Olson's or Graham's statements to the specific uses at issue here, HEI's assertions based on these statements

are no more than mere allegations and do not provide a basis for a hearing.

N. Chemical Changes Caused by Irradiation

The agency considered the chemical changes caused by irradiation and concluded that the chemical differences between foods processed at radiation doses permitted by the regulation and nonirradiated foods are very small and do not affect the safety of the foods (51 FR 13376 at 13377).

HEI stated that:

> BFIFC admitted that new chemicals are formed in foods exposed to ionizing radiation, but did not address the safety of chemicals formed in such foods unless they were "unique to irradiated foods" (51 FR 13377). Harmful chemicals have been identified in foods exposed to ionizing radiation, and some of these chemicals are known to be carcinogenic, such as benzene and formaldehyde. BFIFC ignored the data in the scientific literature and the data submitted in comments responding to the proposed regulation. Data to be presented at public hearings is already part of the Docket Record of FDA, and should have been incorporated into the final regulation.

(HEI Para. I.2.)

There are two aspects to this objection that must be analyzed to determine if HEI has provided the basis for a hearing: (1) The objection's assertion with respect to harmful chemicals being created in irradiated food; and (2) the assertion that BFIFC, or more importantly, FDA, ignored data.

1. Creation of harmful chemicals

Under FDA's regulations and the relevant case law, to present a substantial issue of fact, an objection must do more than make general allegations. It must specifically identify reliable evidence that supports its contentions (21 CFR 12.24(b)(2)). Here, HEI contends that harmful chemicals are formed in food that is irradiated but specifically identifies only benzene and formaldehyde as substances that are formed. Therefore, FDA will consider whether HEI has demonstrated that a substantial issue of fact exists with respect to whether the production of these two chemicals during irradiation affects the safety of the food that is irradiated.

To establish a basis for a hearing, data and information must be submitted that, if established at a hearing, would be adequate to justify resolution of a factual issue in the way sought by the objector and to justify the action requested (21 CFR 12.24(b)(3)). Thus, HEI must provide some basis to find that the levels of benzene or formaldehyde that would be formed in food under the conditions of the regulation raise sufficient concern to affect the conclusion reached by FDA that food irradiated in accordance with 21 CFR 179.26 is safe. Based on its review of HEI's objection, FDA finds that HEI has not done so and, therefore, has not justified a hearing on the effects of benzene and formaldehyde in irradiated food.

a. *Benzene.* HEI has not provided any evidence to show either that benzene is formed in food irradiated under the conditions of the regulation, or that the amount of benzene that might be formed when food is irradiated would be toxicologically significant. Instead, HEI has merely asserted that the entire record previously considered by FDA provides the basis for its contention. Such a general allegation, without any specific evidence to support it, does not provide a basis for a hearing (21 CFR 12.24(b)(2)).

The agency cited a report showing that an increased amount of benzene was found when frozen beef was irradiated in the absence of air at a sterilizing dose, 56 kGy (5.6 Mrad), a level much greater than that permitted by this regulation (Ref. 14). The concentration of benzene in this radiation-sterilized beef was reported as 19 parts per billion (ppb). After cooking, the beef contained 15 ppb benzene, compared to 2 ppb and 3 ppb benzene in cooked beef that has been heat sterilized or frozen but not irradiated. In a 1977 report for the Department of the Army entitled, "Evaluation of the Health Aspects of Certain Compounds Found in Irradiated Beef" (Ref. 14), the Federation of American Societies for Experimental Biology's (FASEB's) Select Committee on the Health Aspects of Irradiated Beef (the Select Committee) stated that much larger amounts of benzene had been found in eggs and refrigerated haddock that had not been irradiated. The Select Committee noted that benzene had also been reported in 20 other nonirradiated foods by numerous workers, but comparison with irradiated samples was difficult because of the lack of quantitative data for the nonirradiated foods.

The Select Committee concluded that the small addition of benzene from radiation-sterilized beef would contribute only a trivial increment to the normal body burden and is unlikely to increase significantly whatever hazard exists from other sources. FDA is not aware of any evidence that would call this conclusion into question, and HEI has not cited any. If benzene is formed in food during irradiation under the conditions of this regulation, FDA would expect the concentration to be far lower than in the radiation-sterilized beef because the permitted dose is less than one-fiftieth of that used with the beef.

b. *Formaldehyde.* The agency does not dispute that formaldehyde may be a secondary reaction product of carbohydrates in aqueous solutions irradiated in the presence of oxygen (Ref. 62). To justify a hearing under 21 CFR 12.24(b)(3), HEI must proffer evidence that formaldehyde: (1) Is carcinogenic when ingested; (2) is formed in food irradiated under the conditions of the regulation; and (3) if formed, is formed in amounts sufficient to raise a health concern. HEI has not provided evidence on any of these three points and thus has failed to justify a hearing.

Formaldehyde is an intermediate in normal amino acid metabolism in the body and is found at the parts per million level in human blood (Ref. 63). Moreover, formaldehyde has been reported to occur in various foods that have not been irradiated, including: red meats, poultry, fish, eggs, cheese, fresh fruits, beer, and soft drinks, generally in the low parts per million range (Refs. 64 to 67). HEI did not state its basis for describing fromaldehyde as carcinogenic, but the agency assumes that HEI is referring to a study in which formaldehyde, administered intranasally to rats, produced carcinomas at the site of application (Ref. 68). The agency previously has concluded that this study is not relevant to the question of whether formaldehyde is carcinogenic when ingested. The agency, in its denial of requests for a hearing on aspartame, concluded that formaldehyde is not carcinogenic when ingested (49 FR 6672; February 22, 1984). HEI has not cited any evidence that would call this conclusion into question and thus has not provided any basis for reconsidering that conclusion.

In the aspartame decision, the agency considered chronic studies in which hexamethylenetetramine was administered to three strains of mice for 60 weeks in drinking water in doses of 0.5 to 5 percent and to Wistar rats in drinking water at 1 percent for 104 weeks. Because hexamethylenetetramine is degraded in the acid medium of the stomach to formaldehyde and ammonia, these studies directly tested whether orally administered formaldehyde is carcinogenic. In the hexamethylenetetramine studies, no evidence of carcinogenic activity was found in any of the test groups (49 FR 6672 at 6680).

In addition, referring to the rat study (Ref. 68) that showed that formaldehyde administered intranasally produced

carcinomas in the nasal cavities, the agency stated: "The site of the carcinomas strongly indicates that the neoplastic process is a localized, not a systemic, reaction to the known irritating and cytotoxic properties of formaldehyde. No increase in tumor incidence was observed at sites remote to direct exposure. The same study supports the further conclusion that direct exposure to relatively high concentrations of formaldehyde gas is necessary before the carcinogenic process occurs" (49 FR 6672 at 6680).

Therefore, with respect to formaldehyde, the agency has not found, and HEI has not cited, any evidence that formaldehyde is carcinogenic when ingested; that formaldehyde is found in irradiated foods at levels significantly different than in nonirradiated food; or that formaldehyde is harmful when ingested at the levels normally found in food. Thus, HEI has not provided any evidence demonstrating that a material issue of fact exists.

2. Whether FDA ignored data

In its objection, HEI stated that "BFIFC admitted that new chemicals are formed in foods exposed to ionizing radiation, but did not address the safety of chemicals formed in such foods unless they were 'unique to irradiated foods' (51 FR 13377)."

HEI's allegation that BFIFC did not address the safety of chemicals unless they were unique is not supported by the administrative record. BFIFC considered both the probable total yield of radiolytic products and the fraction of such products that may be unique before concluding that: "Based on what we have learned from our review of *all* aspects of food irradiation it is apparent that any toxicological testing requirements must *also* be predicated on the amounts of new chemical constituents generated by the irradiation process (URP's)" (emphasis added). Thus, BFIFC considered *all* radiolytic products, not only *new* or unique radiolytic products. A hearing will not be held unless there is a genuine and substantial issue of fact for resolution (21 CFR 12.24(b)(1)), and HEI has failed to show that such an issue exists on this point.

HEI also alleges that "BFIFC ignored the data in the scientific literature and the data submitted in comments responding to the proposed regulation. Data to be presented at public hearings is already part of the Docket of FDA, and should have been incorporated into the final regulation." It should be pointed out that BFIFC's main task was to determine what types of toxicological testing requirements would be appropriate to assure the safety of irradiated foods. BFIFC was a temporary committee that ceased to exist nearly 4 years before FDA issued the proposal that elicited comments on irradiation. Therefore, BFIFC could not have considered data submitted in comments responding to the proposed regulation. However, FDA in its omnibus rulemaking considered not only the BFIFC report, but also other information in the agency's files, including the data submitted with comments to the proposed regulation.

HEI has not identified any specific data that FDA or BFIFC ignored. It has not, for example, cited any studies that were available at the time FDA was considering the omnibus rule, but that the agency failed to consider. A person requesting a hearing must support its allegations with an adequate proffer of evidence. *General Motors Corp.* v. *FERC, supra,* 656 F.2d at 798 n.20. HEI has failed to make such a proffer on this issue and thus has failed to demonstrate that a hearing is appropriate on whether the agency ignored data.

O. Production of Hydrogen Peroxide in Irradiated Foods

In the omnibus rule, FDA responded to a comment that hydrogen peroxide is produced by irradiation and may contribute to carcinogenesis. The agency stated that it had previously considered a Japanese study (Ref. 69) concerning the potential carcinogenicity of hydrogen peroxide and concluded that the evidence does not demonstrate that hydrogen peroxide is a carcinogen (51 FR 13376 at 13379; see also 46 FR 2341; January 9, 1981). FDA further noted that any hydrogen peroxide formed would be rapidly degraded by natural enzymes and antioxidants in food, and that any residual hydrogen peroxide, if present, would be considerably less than that encountered ordinarily in foods and environmental sources.

HEI stated:

> The FDA admitted "the formation of detectable quantities of hydrogen peroxide, organic peroxides, and hydroperoxides during irradiation of foods in the presence of oxygen," but erroneously claimed that such peroxides would disappear before food consumption (51 FR 13379). While the FDA might regard the Japanese study finding duodenal cancer caused in C57B mice by hydrogen peroxide as inconclusive, the FDA offers no *evidence* to disprove the study findings. Further evidence regarding the dangers of peroxides will be offered at the public hearing, along with the reasons for considering the Japanese study important.

(HEI Para. I.7.) (Emphasis by HEI.)

This objection raises the question of the extent to which FDA may rely on the determination that it made in the 1981 rulemaking that hydrogen peroxide has not been shown to be a carcinogen. A similar question was raised in *Community Nutrition Institute* v. *Novitch,* 773 F.2d 1356 (D.C. Cir. 1985). In that case, in the course of challenging FDA's approval of the use of aspartame in ready-to-drink beverages, the objector also challenged the agency's approval of certain dry uses of aspartame. The court rejected the latter challenge, stating: "The agency's conclusions concerning the safety of the dry use of aspartame, except to the extent that new evidence suggests that the FDA may not rely on these prior findings in its deliberations on wet use, may not be raised again in this proceeding in the interests of administrative finality and judicial economy." (*Id.* at 1362–1363.)

Consequently, in this proceeding, the agency can rely on the findings that it made about hydrogen peroxide in earlier rulemakings except to the extent that new evidence that raises questions about the agency's conclusion is presented.

The agency subjected the data from the Japanese study cited by HEI to an in-depth analysis in its final decision on the safe use of hydrogen peroxide as a sterilizing agent for food packaging materials (46 FR 2341; January 9, 1981). After review, including consultation with the authors of the study, the agency concluded that the results of the study did not provide sufficient evidence to designate hydrogen peroxide as a carcinogen. FDA placed the manuscripts of the Japanese study and memoranda of FDA's Cancer Assessment Committee on public display in the Dockets Management Branch under Docket No. 79F–0318.

In addition, FDA has recently completed its review of whether hydrogen peroxide is generally recognized as safe (GRAS) for direct addition to food (51 FR 27169; July 30, 1986). The agency discussed the Japanese study in its November 17, 1983, GRAS proposal (48 FR 52323).

For the objector to raise a material question of fact about the safety of hydrogen peroxide, it must point to evidence that is inconsistent with FDA's conclusions. Yet, HEI has not provided any information to support its claim that hydrogen peroxide is carcinogenic, or that other peroxides are present in irradiated foods in hazardous amounts. While, as stated above, FDA has the ultimate burden of proof when it approves the use of a food additive, once the agency makes a finding of safety in a listing document, the burden shifts to an objector to come forward

with evidence that calls into question FDA's conclusion. HEI has failed to present any such evidence. *American Cyanamid Co.* v. *FDA, supra,* 606 F. 2d at 1314–1315. Rather, HEI merely promised to provide further evidence at a hearing on the dangers of peroxides and on a study that FDA had previously evaluated in depth in a proceeding in which no one requested a hearing.

A hearing cannot be justified on the basis of a promise that some unidentified evidence will be provided at the time of that hearing. The person seeking a hearing must meet a threshold burden of tendering evidence that suggests the need for a hearing. *Costle* v. *Pacific Legal Foundation, supra,* 445 U.S. at 214. As discussed above, HEI has not proffered any evidence on hydrogen peroxide to challenge the agency's conclusion that food irradiated under the conditions of the regulation is safe. Thus, a hearing on this objection is denied.

In addition, HEI's statement that FDA * * * erroneously claimed that such peroxides would disappear before food consumption (51 FR 13379) * * * " is a bald assertion, without any proffer of evidence to support it. HEI has not cited any evidence that hydrogen peroxide would remain in irradiated food at significant levels. A hearing will not be granted on the basis of mere allegations or denials (21 CFR 12.24(b)(2)). Thus, HEI has failed to justify a hearing on this point.

P. Radiolytic Products

BFIFC stated that radiolytic product generation is dependent primarily upon the amount of energy absorbed by the food. Based on a review of available literature identifying and quantifying substances produced in foods by radiation, BFIFC estimated that irradiation of food at 1 kGy would generate approximately 30 parts per million of radiolytic products. BFIFC used experimental data on irradiated and nonirradiated food to estimate that approximately 90 percent of the radiolytic products identified were known natural food components and noted that the remaining 10 percent were chemically similar to known natural food components (51 FR 13376 at 13378). Based on the findings of BFIFC and the Task Group, and on its review of the other information in the administrative record of the omnibus proceeding, FDA concluded that food irradiated under the conditions of the regulation is safe (51 FR 13376 at 13378).

1. Effect of irradiation on pesticide residues

In response to a comment about the fate of pesticide residues on produce, the agency concluded that the total amount of radiolytic products from pesticide chemicals on foods that are irradiated will be virtually nil, and that these radiolytic products do not pose a hazard to health (51 FR 13376 at 13380).

HEI stated that:

> The FDA admitted that a pesticide chemical present on irradiated food could be chemically changed by the irradiation process (51 FR 13360) [sic]. The FDA offered no scientific evidence regarding the types of changes that might be expected, but a mere "guess" or "estimate" regarding the parts per million to be found in food. This is equivalent to guessing that a potential hazard is harmless, and does not carry out the FDA mandate to assure safety. Further evidence regarding these dangers and the FDA failure to assess them will be offered at the public hearing.

(HEI Para. I.8.)

(See Objection No. 159 in Docket.)

To justify a hearing, an objector must meet a threshold burden of tendering evidence suggesting a need for a hearing. *Costle* v. *Pacific Legal Foundation, supra,* 445 U.S. at 214. It must point to facts that provide a basis on which to question the agency's conclusions. *Cerro Wire & Cable Co.* v. *FERC,* 677 F.2d 124, 129 (D.C. Cir. 1982). Here, to raise questions about FDA's conclusions, HEI would have to point to some evidence that would lead one to conclude that degradation products are more toxic than the pesticide itself, and that the amount of degradation products is sufficient to make a difference in the toxicity of the resulting residue mixture. HEI has not proffered any evidence, however.

Although HEI promises to offer evidence at a hearing, a hearing cannot be justified on the basis of a promise that some unidentified evidence will be provided at the time of a hearing. A person requesting a hearing must support its allegations with an adequate proffer of evidence. *General Motors Corp.* v. *FERC,* 656 F.2d 791, 798 n.20 (D.C. Cir. 1981). Rather than presenting evidence, HEI asserts that FDA did not adequately justify its conclusions. Such an assertion will not justify a hearing. While, as stated above, FDA has the ultimate burden of proof when it approves the use of a food additive, once the agency makes a finding of safety in a listing document, the burden shifts to an objector to come forward with evidence that calls into question FDA's conclusion. *American Cyanamid Co.* v. *FDA, supra,* 606 F.2d at 1314–1315. HEI has failed to present any such evidence. Thus, it has not provided any basis for a hearing.

2. Metabolism of radiolytic products

One objection to the omnibus regulation which did not request a hearing took exception to FDA's response to a comment concerned that highly toxic unidentified radiolytic products may be present at low concentrations. The objector cited FDA's response and objected as follows:

> P. 13386—"Such URP's may be free radical coupling products of lipid and protein-derived radicals, dimers, and cross-linked products. However, enzymatic hydrolysis * * * by normal digestive enzymes is expected to yield normal molecular subunits such as fatty acids, amino acids, monosaccharides * * *." Many of the coupling products may involve carbon-carbon bonds that are not degraded by digestive enzymes.

(See Objection No. 159 in Docket.)

The agency has considered this objection and has found it to be without merit. The objector has misrepresented the agency's analysis on coupling products by omitting the words "of some of these compounds." The agency stated in the omnibus rule that URP's may be formed, including some that are structurally atypical of parent molecules, such as free radical coupling products of lipid and protein-derived radicals, dimers, and cross-linked products, and that *some* of these would be digested normally (51 FR 13376 at 13386). BFIFC had concluded that enzymatic hydrolysis of such radiolytic products by digestive enzymes would metabolize the majority of such radiolytic products to yield normal molecular subunits, such as fatty acids, amino acids, and other components that would result normally from the digestion of the parent molecules (Ref. 5). Neither the agency nor BFIFC said or implied that all coupled or crosslinked products would be digested to normal components. BFIFC's analysis did show, however, that while it was assuming coupled products to be unique, most of these products would be metabolized in the same way as other food components, and the amount of products with uncharacterized toxic potential would be reduced considerably.

Therefore, the objector has not pointed to any problem in the agency's position but has focused on the production of possible unique radiolytic products. The agency did consider the possible production of such products and concluded that the possibility of their formation would be extremely low, and that they would be virtually impossible to detect toxicologically (51 FR 13376 at 13378).

As noted in the omnibus rule (51 FR 13376 at 13379), the important issue that the agency has had to consider is the probability that a toxic radiolytic end-product will be formed in sufficient amounts to make the food unsafe. The agency's review of hundreds of animal feeding studies produced no evidence of the presence of radiolytic products in toxic amounts in foods radiated under conditions consistent with those permitted under the omnibus rule. This failure to find toxic amounts of radiolytic products supports the agency's conclusion on safety. The objector has provided no information to challenge this conclusion.

3. Toxicity of radiolytic products

One objection to the omnibus regulation which did not request a hearing took exception to FDA's discussion of the usefulness of the toxicological studies that the agency reviewed:

P. 13384—"* * * if a potent toxic material were present at any level of toxicological significance in irradiated foods ingested by test animals, some consistent toxicological signs would be manifest in the studies." Why? These studies you reviewed covered a wide variety of foods, tested animals, dosages of radiation used, diets used, etc. One should *not* expect consistent toxicological signs. On p. 13380 you state "* * * radiolytic products from different spices are likely to be different." The same is true of different fruits and vegetables, so the toxicological effects would be expected to be different here too. Don't you think so?

(See Objection No. 159 in Docket.)

Most foods, including those tested in animal feeding studies, are composed mainly of water, carbohydrates, fats, and proteins as well as lesser amounts of vitamins, minerals, and a large variety of flavoring components. Because the same constituents dominate the composition of many foods, one would expect similar products from foods with similar composition.

The major reaction resulting from irradiating foods that have a significant water content, such as fruits and vegetables, involves reaction of free radicals of water with other food constituents, such as carbohydrates. Thus, while it is true that if a potent toxicant were formed in irradiated food, its toxic significance would not be the same at all doses or in all foods, it does not follow that if a potent toxicant were present in irradiated food, there would be no correlation among the studies FDA reviewed. Therefore, because FDA reviewed a large amount of animal feeding study data, a potent toxicant should have shown some pattern in similar studies with similar foods. FDA did not see such a pattern.

Because the data from tests with a wide variety of foods at a variety of doses do not provide evidence of a potent toxic material, the likelihood of finding a toxic effect with food irradiated under the limited conditions permitted by this rule is so small as to be insignificant. The objector has merely disagreed with the agency's conclusion and has not provided any evidence to the contrary.

Q. Test for Quantity of Radiolytic Products in Food

HEI stated:

FDA has not developed an empirical test for measuring effectively the quantities of residual toxic radiolytic products and unique radiolytic products present in irradiated foods. FDA should withdraw its regulation until research into developing such a test, currently underway at the National Bureau of Standards, is completed. Evidence regarding this issue and the work underway at NBS will be presented at the public hearing.

(HEI Para. I.4.)

Under FDA's regulations, a hearing will not be granted on factual issues that are not determinative with respect to the action requested (21 CFR 12.24(b)(4)). HEI has failed to point to any specific way in which the rule itself is inadequate without a test. HEI has not explained what it means by "an empirical test," what such a test would accomplish, or what allegedly toxic or unique radiolytic products require quantitative measurement. Thus, HEI has not provided a basis for a hearing.

Furthermore, HEI has not provided any basis to find that the work done at the National Bureau of Standards (NBS) is relevant to this proceeding. The work conducted at NBS was a research project funded by USDA in 1986. This project was directed primarily at developing an analytical method for determining whether poultry has been irradiated. The project involved detection of a radiolytic product of an amino acid found in proteins. It was not designed to be applicable to the foods covered by this regulation.

R. Possible Synergistic Effect

A synergistic effect is an action by two or more substances to produce an effect that each substance is incapable of producing by itself. Such an effect can be beneficial or detrimental. The agency does not ordinarily consider hypothetical synergistic effects unless there is reason to believe that there will be synergistic effects that present a safety concern. It did not consider such effects in this rulemaking because available evidence did not suggest that there are any such effects.

HEI stated that:

The FDA fails to address the potentially synergistic effects of new chemicals created by the food irradiation process in different foods [sic] items that might be ingested by an individual. Evidence of such synergistic effects would be presented at a public hearing.

(HEI Para I.10.)

HEI has not presented any evidence to show that there is any likelihood that synergistic effects will occur among the chemicals created in food by irradiation. Rather, HEI's request for a hearing merely alleges that such effects will occur, without providing any supporting evidence other than a vague offer to present evidence at the hearing. Mere allegations are insufficient to justify a hearing. An objector must make an adequate proffer of evidence to support its allegations and to show that they provide a basis on which to call into question the agency's conclusions. *Cerro Wire & Cable Co.* v. *FERC,* supra, 677 F. 2d at 129.

Moreover, a hearing cannot be justified on the basis of a promise that some unidentified evidence will be provided at the time of that hearing. The person seeking a hearing must meet a threshold burden of tendering evidence that suggests the need for a hearing. *Costle* v. *Pacific Legal Foundation,* supra, 445 U.S. at 214. By merely making the bald assertion that the possibility of synergistic effects exists and by failing to submit any evidence to support that assertion, the objector has failed to demonstrate that an issue of fact exists with respect to the possible synergistic effects of radiolytic products and thus has failed to justify the granting of a hearing.

FDA is not aware of any evidence that radiolytic products produce synergistic effects. FDA stated in the omnibus rule that experiments have shown that very few, if any, of the radiolytic products are unique to irradiated foods (51 FR 13376 at 13378). One can speculate on possible synergism among any of the thousands of chemical components that are naturally present in the daily diet, but unless one has reason to believe that a particular effect may occur, such speculation is likely to be fruitless and, therefore, an inappropriate subject for study. HEI has not provided a plausible hypothesis or appropriate information that would lead one to suspect adverse synergistic effects from components of irradiated foods.

S. Induced Radioactivity: Sodium-24

One objection to the irradiated pork rule stated that when pork has been irradiated, sodium-24 becomes a pure gamma emitter in the pork for 24 hours after treatment, thereby creating a dangerous situation for 24 hours. The objector did not submit any data to support this objection, nor did it request a hearing.

The agency has considered this objection and has found it to be without merit. FDA stated in its 1981 advance notice of proposed rulemaking that "the use of ionizing radiation of appropriate source energy does not induce any detectable radioactivity in foods when measured by methods that can easily detect the presence of radioisotopes that occur naturally in foods" (46 FR 18992; March 27, 1981). The report that served as a basis for this statement (Ref. 70) noted that sodium-24 can be produced and measured in foods when they are irradiated by sources with energy levels in excess of 12 million electron volts (MeV) but not after irradiation by sources of 10 MeV or less. The agency has limited the use of sources of radiation to those that produce radiation at energies of 10 MeV or less (21 CFR 179.26(a)). The radiation energies of cobalt-60 and cesium-137 are both below 2 MeV. The agency is not aware of any evidence to demonstrate that irradiation of pork under the conditions of the regulation produces measurable amounts of sodium-24.

T. Summary

In this section on safety, the agency has addressed objections to its conclusion that foods irradiated under the conditions of the regulation are safe.[6] The agency has considered these objections and finds that none of them justifies a hearing under the criteria outlined in 21 CFR 12.24(b). Thus, the agency is denying all of the objections and requests for a hearing on the safety of the irradiation of food under the conditions set forth in 21 CFR 179.26.

III. Effect on Nutritional Quality

As stated earlier, some changes in food chemistry occur during irradiation processing. Such changes can occur in nutrients as in other components of food. Although certain nutrients in particular food commodities are extremely sensitive to irradiation, there would not be a significant effect on a consumer's diet from food irradiation unless the consumer depended on a particularly sensitive food for a major portion of the dietary need for a particularly sensitive nutrient. Just as with other processing methods, the nutritional consequences of irradiating a food must be evaluated by considering the likely effect on the diet as a whole.

As a comparison, the freezing process is probably the best preservation method for retention of vitamin content; however, this method is not without some effect on the processed food. For example, some vegetables lose up to 14 percent of vitamin C and from 3 to 8 percent of thiamine when frozen. In the case of pork chops, an excellent source of thiamine, losses in this vitamin following 6 months of frozen storage have been reported to range from an insignificant amount to as much as 40 percent (Refs. 71 and 72).

Before freezing, most vegetables are blanched to inactivate enzymes that would otherwise cause unacceptable changes in sensory properties and nutritive value during frozen storage. Losses of vitamin C during water blanching and cooling of eight common vegetables (e.g., green beans, broccoli, and spinach) range as high as 70 percent, with an average loss of around 25 percent. Losses of thiamine in some of these same vegetables range as high as 80 percent.[7]

Nevertheless, although some nutrient losses occur during processing, one would not say that freezing renders such foods to be nutritionally unwholesome or unsafe. The same criteria for determining safety and wholesomeness must be applied to processing by irradiation.

Any change caused by irradiation will be dose dependent, so that the significance becomes less as the dose gets smaller. The agency cited several references in its proposal (49 FR 5714 at 5721) that demonstrate that there are no significant nutrient differences between nonirradiated foods and foods irradiated at a dose below 1 kGy (100 krad). FDA agreed with those reports and concluded that nutritional variations in foods irradiated under the conditions of the regulation are nearly always negligible and therefore of no significance to human health. Because the agency considered food irradiated under the conditions of the regulation to be no different nutritionally from nonirradiated foods, and because no comment submitted evidence to the contrary, the agency concluded that destruction of nutrients was not an issue in this rulemaking (51 FR 13376 at 13381).

HEI stated that:

> Nutrient destruction is generally admitted regarding exposure to ionizing radiation, but the FDA states that there is no nutritional difference between unirradiated food and food irradiated at levels below 100,000 rads (51 FR 13381). This claim is false, and relevant evidence will be submitted at the public hearing. For example, an initial study conducted at the USDA's Eastern Regional Research Center in Philadelphia found that pork irradiated at 100 krads suffered a 20% loss of thiamine. Since nutrient loses at doses higher than 100 krads are usually dose related and are well documented (See Exhibit A, Tony Webb, "Food Irradiation in Britain" pp. 14 & 15), it is unreasonable to claim that losses magically disappear at lower levels.

(HEI Para. I.11.)

On February 2, 1987, FDA requested that HEI submit the information that it intended to present at a hearing to support its contention that nutritional differences in food irradiated under the conditions of the regulation are significant. In its reply of March 6, 1987, HEI cited 10 documents but did not include copies of any of those documents. Seven of the documents that HEI cited were on the effect of irradiation on vitamins and other nutrients, including natural antioxidants; two articles were on the effect of irradiation on fats; and one reference discussed nutritional loss as a function of dose. FDA searched its files for the documents mentioned by HEI and was able to locate all but two. On May 5, 1987, the agency again wrote to HEI and requested the two references that were not available in the ageny's files. HEI provided one of the references but was unable to locate the second.

A. Original Objection

In its objection, HEI challenged FDA's statement in the omnibus rule that "* * * the available literature indicated that there are no nutritional differences between unirradiated food and food irradiated at levels below 1 kGy (100 Krad) * * *" (51 FR 13376 at 13381). It is not clear, however, whether HEI is claiming that irradiation of some foods will reduce the amounts of some nutrients, or that foods irradiated under the conditions of this regulation will adversely affect the nutritional status of humans who consume these foods. FDA did not intend to imply that there are never changes in nutrient levels when food is irradiated. FDA's statement was intended to mean that the nutrient losses below 1 kGy are so small as to be of no nutritional consequence for the human diet. Because the amount of chemical change is directly proportional

[6] HEI made 21 specific objections on safety, each of which, it claimed, justified a hearing. HEI made a 22d objection on the nutritional quality of irradiated foods. This objection is discussed in the next section.

[7] Many papers have been published to document such results. A succinct summary in tabular form is contained in Ref. 73.

to dose, it is reasonable to conclude that some fraction of the nutrients may be lost at any dose, and that the amount lost will approach zero as the dose approaches zero. FDA has never claimed "that losses magically disappear at lower levels * * *" as HEI apparently asserts in its objection.

To justify a hearing on this point, it is not enough for HEI to simply assert that some nutrient loss can occur. HEI must present evidence that suggests that nutrient losses in food irradiated at doses permitted by the regulation are sufficiently large and would so affect the diet that such food would be nutritionally unwholesome or unsafe. A hearing will not be held unless resolution of a factual issue in the way sought by the objector is adequate to justify the action requested (21 CFR 12.24(b)(4)).

In its objection, HEI stated that an unpublished USDA study "* * * found that pork irradiated at 100 Krads suffered a 20% loss of thiamine." HEI has neither provided any evidence from such a study nor provided any basis for why its statement, if true, would show that irradiated pork is unsafe. A hearing will not be held unless a factual issue can be resolved by specifically identified reliable evidence (21 CFR 12.24(b)(2)).

HEI also stated that other "* * * relevant evidence will be submitted at the public hearing * * *." As stated above, FDA requested that HEI submit the information it intended to present, and HEI responded by citing 10 documents. These documents and the questions they raise are considered below.

B. Effect on Nutrients

Seven of the documents HEI cited referred to the possible loss of nutrients, such as vitamins, when food is irradiated. HEI cited one reference (Ref. 50) on the effects of irradiation on the vitamin C content of orange juice, one reference on the effects of irradiation on *beta* carotene in solution, and one reference to an unpublished USDA study on the thiamine content of irradiated bacon in the raw, cooked, or freeze-dried form. HEI stated that:

> Ascorbic acid losses in orange juice amounted to 10% to 70% after irradiation with 2.5 to 10.0 kGy according to Beyers, M. et al., "Chemical Consequences of Irradiation of Subtropical Fruits," in P.S. Elias and A.J. Cohen, ed's, RECENT ADVANCES IN FOOD IRRADIATION, 171 at 178 (1983).

(HEI March 6, 1987, response, p. 3 (Ref. 2).)

> Snauwaert, F. et al., "Influence of Gamma Irradiation on the Provitamin A (Beta-Carotene) in Solution," in RADIATION PRESERVATION OF FOOD, IAEA & FAO: Vienna, 29 (1973). Table II demonstrates dose related reduced Beta-carotene at doses ranging from 3.36 to 285 krad. The researchers stated, "At doses higher than 200 krad Beta-carotene tends to degrade completely."

(HEI March 6, 1987, response, p. 4 (Ref. 2).)

> A recent report submitted to USDA's Food Safety and Inspection Service by the Agricultural Research Service reported that "thiamine content of bacon in raw, cooked, or freeze-dried form degraded at a significantly higher rate during cooking if the bacon had been irradiated," according to *Food Chemical News* 42 (Nov. 10, 1986). We have not yet obtained a copy of this report, but we believe that it should be considered by FDA.

(HEI March 6, 1987, response, p. 3 (Ref. 2).)

> HEI cited testimony before Congress, on behalf of the National Nutritional Foods Association, on a bill to provide Federal coordination for the continued development and commercialization of food irradiation. The testimony claimed that irradiation would reduce the concentration of natural "protective materials," such as antioxidants, in proportion to the radiation dose and operating conditions.

(HEI March 6, 1987, response, p. 4 (Ref. 2).)

> HEI also cited three review articles that discuss loss of vitamins and other nutrients in irradiated foods.

> Dennison, R.A. and E.M. Ahmed, "Review of the Status of Irradiation Effects on Citrus Fruits", from PROCEEDINGS OF THE INTERNATIONAL SYMPOSIUM ON FOOD IRRADIATION, June 6–10, 1966, IAEA/FAO, 619 at 627 (1967). Vitamin C losses indicated by several studies are summarized at p. 627.

(HEI March 6, 1987, response, p. 3 (Ref. 2).)

> Murry, T.K.[sic], "Nutritional Aspects of Food Irradiation," presented to the Joint FAO/IAEA/WHO Expert Committee on the Wholesomeness of Irradiated Food, Oct. 27-Nov. 3, 1980. This paper cites a variety of studies evaluating nutritional aspects of irradiated food. It admits that nutritional losses occur at low doses, but dismisses them by stating that they are less than those found with other food processes. Canned foods are well known to be nutritionally depleted, and the consumer can readily tell that a food was canned since it is purchased in a can or jar. Irradiated food can be sold as "fresh," with only a misleading symbol, after April 18, 1988, and consumers are unlikely to realize that the food is processed and that vitamin content is reduced. Murry reported that Azar observed losses of up to 22% in thiamine as well as riboflavin, niacin, and pyridoxine in rice.

(HEI March 6, 1987, response, p. 3 (Ref. 2).)

> Vakil, Urmila K. et al., "Nutritional and Wholesomeness Studies with Irradiated Foods: India's Program," RADIATION PRESERVATION OF FOOD, IAEA & FAO: Vienna 673 (1973). Table IV shows losses in nutrients when wheat is irradiated at doses of 20 krad and 200 krad. They found that 8 to 12% of total thiamine, riboflavin and niacin were lost due to radiation treatment. Up to 25-35% of alpha-tocopherol, localized in the germ, was lost with radiation doses of 20 and 200 krad. An overall increase of about 8% in free amino acid levels was observed on irradiation up to 1 Mrad. Ionizing radiation caused fragmentation of the starch and proteins in wheat. B vitamins were reduced in irradiated shrimp.

(HEI March 6, 1987, response, p. 5 (Ref. 2).)

The issue raised by HEI must be a material issue concerning which a meaningful hearing might be held. *Pineapple Growers Ass'n of Hawaii* v. *FDA*, supra 1085. As discussed above, the agency recognizes that irradiation can produce nutrient losses under some conditions but has concluded that such effects are not a safety concern under the conditions of the regulation.

To justify a hearing, HEI must provide evidence that nutritional loss in a food irradiated under the conditions of this regulation either renders the food unsafe or has a significant effect on the diet of humans (see 21 U.S.C. 348(c)(5)(B)). While, as stated above, FDA has the ultimate burden of proof when it approves the use of a food additive, once the agency makes a finding of safety in a listing document, the burden shifts to an objector to come forward with evidence that calls into question FDA's conclusion. *American Cyanamid Co.* v. *FDA*, supra, 606 F. 2d at 1314–1315.

Despite the fact that it referenced numerous documents, HEI has submitted no information to support its allegation that nutritional differences in food irradiated under the conditions of the regulation are significant to human health and are a safety concern. For example, in the first three studies cited above, none of the foods discussed can be irradiated under the conditions of the regulation.

The statement of the National Nutritional Foods Association cited by HEI contends that "antioxidants" occurring naturally in food are chemically consumed in reaction with other radiolytic products. However, either the authors of the statement nor HEI has provided evidence to support the contention that irradiation of food under the conditions of the regulation will result in a significant reduction in these "protective materials" or to show that any reduction that might occur would be detrimental to the consumer.

The other three articles cited by HEI are compilations of data from many studies. None of these authors concluded that losses of nutrients from foods irradiated at doses permitted by the regulation are of any significance to human health. For example, HEI cites Murray as stating that nutritional losses "are less than those found with other food processes." [8] Another of these cited authors (Vakil) concluded that "[c]ompositional changes and nutritional losses due to irradiation are comparable to those caused by conventional processing methods * * *." HEI has not provided any rationale to show why these articles would support its contention that losses of nutrients from foods irradiated under conditions permitted by the regulation would render the food unsafe or have a significant effect on human health. Thus HEI has not provided any basis for a hearing.

Moreover, HEI's statement that "* * * consumers are unlikely to realize that the [irradiated] food is processed * * *" is not true. The agency requires that the labeling of an irradiated food must state that the food has been irradiated (21 CFR 179.26(c)). (See also IV. Labeling).

C. Effect on Fats

HEI cited two references on the toxicity or indigestibility of fats with high peroxide values (rancid fats) (Refs. 75 and 76).

Draybill [sic], H.F., "Nutritional and Biochemical Aspects of Foods Preserved by Ionizing Radiation," 50 J. HOME ECONOMICS 695 (Nov. 19, 1958) citing Andrews, J.S., Mead, J.F., and Griffith, W.H., "Toxicity of lipid peroxides in the rat," 15 FED. PROC. 918 (1956), states, "Highly peroxidized oils (peroxide number of 3,000) produced by irradiation and oxidation are toxic when fed to rats at 20 per cent level in diet, but fats of lower peroxide numbers (peroxide number below 400) when fed at same level in a diet to rats were nontoxic and maintained normal growth (8)." The nutritive value of the macronutrients is apparently adversely affected.

Schreiber, Manuel, and E.S. Nasset, "Digestion of Irradiated Fat in Vivo," 14 J. APPLIED PHYS 639 (1959) concluded that "irradiation of lard is detrimental to digestion in the dog." This study found that irradiation increased the peroxide value of lard from 1–2 to 176, and that in 14 months of cold storage the peroxide value continued to rise. The damaged irradiated fats apparently caused poor digestion, with irradiated lard failing to leave the stomach in normal time periods.

(HEI March 6, 1987, response, p. 3 (Ref. 2).)

Neither of these studies provides a basis for a hearing. Both studies are directed to the health effects of fats and oils with high peroxide content (rancid fats). The toxicity or indigestibility of rancid fats is not in dispute, however.

Peroxides are produced in fats by a variety of means, including heating and storage as well as by irradiation in the presence of air. HEI has not provided any reason to believe that rancidity is a consequence of irradiating foods under the conditions of this regulation. However, even if irradiation causes rancidity of foods, this fact would not cause the agency to change its conclusion. Foods with a high fat peroxide content (rancid fats) are not eaten because they are unpalatable. It is unlikely that any food that would become rancid when irradiated would be irradiated because such an irradiated food would not be marketable. Therefore, these studies would not provide a basis for finding irradiation to be unsafe and thus do not provide a basis for granting a hearing under 21 CFR 12.24(b)(4).

D. Control of Dose

HEI stated that:

While setting an upper limit of 100,000 rads for food preservation helps limit nutrient losses due to radiation (since nutrient losses increase with dose), in practice, it is quite possible that foods will get even higher doses than planned. In a petition to the FDA to allow higher irradiation doses for spices (3,000,000 rads), R.L. Hall, Vice President—Science & Technology of McCormick & Company, Inc., stated, "In existing large-scale irradiators, it is quite likely that an overdose of up to 250% can be expected." Control of dose is clearly not as simple as it sounds. Measurable losses of food nutrients at doses higher than 100,000 rads may suggest losses occurring at lower doses, whether or not these losses are easily measured.

(HEI March 6, 1987, response, p. 2 (Ref. 2).)

HEI appears to misunderstand both the requirements of the regulation and the practical significance of the variation in dose during processing. In its proposal, FDA discussed the dose variation that a given bag, barrel, or pallet of food receives during irradiation. In an example, it stated that in a typical use application, one portion of the container may receive three times (or 300 percent) as much radiation as the portion receiving the smallest dose (49 FR 5714 at 5717). Hall's statement refers to the need for a margin 250 percent above the minimum dose, similar to FDA's estimate. The petition that HEI refers to requested that the maximum dose be set high enough to allow a minimum dose that is effective. The dose of 1 kGy (100,000 rads) permitted by this regulation is the maximum dose allowed for foods that are sources of nutrients, not the minimum. Because of the variation in dose at different positions of a container during irradiation, treatment to a maximum dose of 1 kGy means that other portions of the container are likely to receive less than 0.5 kGy and the overall average dose is likely to be less than 0.75 kGy. Thus, food irradiated under the conditions of the regulation will not receive a dose greater than the maximum allowed. In fact, on the average, food will receive a considerably lower dose than that permitted by the regulation, not a higher dose.

HEI has not provided any evidence that any food irradiated under the conditions of the regulation will receive a dose of radiation that is greater than that allowed. Thus, there is no issue of fact in dispute for resolution at a hearing (21 CFR 12.24(b)(2)).

IV. Labeling

In the omnibus rule, the agency required wholesale and retail labeling of all food that has been irradiated (first generation food) because the irradiation of food, like other processing, could affect its organoleptic characteristics. The agency did not require special retail labeling for an irradiated ingredient in a multiple-ingredient food (second generation food) because such a food has obviously been processed, and the effects of radiation on individual ingredients would likely have no significant effect on the final product (51 FR 13376 at 13389).

A. Use of Term "Ionizing"

One objection to the omnibus final rule, which did not include a request for a hearing, stated that because infrared, ultraviolet, and visible radiation, as well as microwaves and radiowaves, are all nonionizing forms of radiation, labeling the food as treated "by irradiation" or "with radiation", without stating the type of radiation, misleads the consumer. The objector stated that "[i]t is clearly hypocritical of the FDA to say it encourages consumer education but not require it in the form of explicit labels stating that the radiation is *ionizing*."

The objector is correct that there are several forms of radiation, not all of which are ionizing. However, requiring the use of unfamiliar technical terms

[8] HEI also cited an article by Azar (Ref. 74), referenced by Murray, that reported 22 percent loss of thiamine and other vitamins in irradiated rice, without reporting the dose applied. HEI did not provide a copy of this study when FDA requested it for review. In the absence of this article, the agency cannot evaluate this evidence. A reference to information that is not available cannot serve as a basis for a hearing to consider such information.

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does not necessarily convey useful information to most consumers. The word "radiation" is commonly used for the type of radiation emitted by radioactive matter or by X-ray machines, i.e., ionizing radiation. The agency chose to require only this simple term on a label because the agency felt that it would inform the consumer at least as well as the more technical terminology (51 FR 13376 at 13387).[9] The objector did not provide any evidence that the additional word would increase the understanding of most consumers. However, the agency does permit the manufacturer to state specifically the type of radiation used in the treatment, e.g., "Treated with ionizing radiation," or "Treated with gamma radiation," if the more specific description is indeed applicable (51 FR 13376 at 13388).

B. Petition to Reconsider the Labeling Statement

The agency received a petition to reconsider the labeling provisions and decided to treat that petition as an objection because FDA received it within the 30 day objection period. The objector (Docket No. 81–N0004/PRC) argued in its objection that the required statement "Treated with radiation" is misleading. He provided data from a limited consumer survey as the basis for proposing that the required statement be replaced by the word "picowaved" or "irradiated".

In this consumer survey, consumers in one city were asked whether they would think that food that was labeled "treated with radiation" contained radiation, and whether they would buy such food. Consumers in another city were asked the same question except the term "ionizing radiation" was used on the hypothetical label. A majority of respondents stated that they would not buy food labeled in this way because it might be radioactive. No consumers were asked about their understanding of the words "picowaved" or "irradiated."

The agency recognizes that many consumers do not understand the meaning of the word "radiation," but it believes that any confusion created by use of the terms "radiation" or "irradiation" can be corrected by proper consumer education. The petitioner provided no evidence that the phrasing requested would be more informative than that required by the regulation. Therefore, FDA rejects this request.

[9] FDA does not require a statement that the food has been irradiated on foods treated by nonionizing radiation. Therefore, there should be no confusion of terms.

C. Retail Labeling

1. Label statement

Several objections to the irradiated pork rule stated that the label for pork treated with radiation should so indicate and objected that the regulation did not require special labeling. One of the objectors requested a hearing.

These objectors are confused about what the irradiated pork rule did. It amended 21 CFR 179.22(b) by adding pork to the list of foods that may be irradiated. Paragraph (c) of 21 CFR 179.22 required the statement "Treated with gamma radiation"on labels of irradiated food. The irradiated pork rule did not exempt pork from the labeling requirement in 21 CFR 179.22(c). Thus, the objections to the irradiated pork rule were wrong in concluding that the regulation did not require special labeling.

Section 179.22(c) was superseded by the omnibus rule, which also establishes labeling requirements for all irradiated foods. Thus, under the former 21 CFR 179.22 or the current 21 CFR 179.26, labels of irradiated pork must state that the food has been irradiated. Consequently, these objections raise no issue to be resolved at a hearing.

2. International logo

One objector, the petitioner for the irradiated pork regulation, requested that the international logo for irradiation be used as an alternative to specific wording required by 21 CFR 179.22(c).

The agency concluded in the omnibus rule that an internationally used logo should be placed on labels and labeling, along with specified wording that would explain the meaning of the logo to consumers until the logo became readily recognized. Underlying this action is a finding by the agency that consumers are not aware of the meaning of the logo, and that it would therefore not be appropriate at this time to place the logo on a food label without an appropriate explanation. The objector has not presented anything other than a mere assertion that the logo is an appropriate alternative to the wording required by the agency. Therefore, the agency rejects this alternative.

3. Two year "sunset clause"

Several objections to the omnibus rule expressed opposition to a 2-year "sunset clause" for the required label statement that accompanies the international, or "radura," logo. They claimed that the logo, by itself, is misleading and will not provide the needed information to the consumer. The objectors said that it is unrealistic to expect all consumers to become informed about the logo in a 2-year period, and that the use of the logo alone would be objectionable. Some of the objectors requested a hearing.

On February 18, 1988, the agency published a proposal to extend the wording requirement (52 FR 4856) and provided 30 days for comment on this proposal. On April 18, 1988, the agency published a final regulation that discussed all comments and extended the wording requirement another 2 years until April 18, 1990 (52 FR 12756). Thus, the agency has agreed that 2 years was too short a time for the wording requirement and has amended the regulation accordingly. Consequently, these requests for a hearing are moot.

D. Ingredient Labeling

Several objections were opposed to irradiation of an ingredient without requiring special labeling on all foods that contain that ingredient. Some of the objectors requested a hearing on whether FDA should require ingredient labeling. The most comprehensive statement of this objection was submitted by HEI, which stated that:

> The FDA ably defends its decision to label irradiated foods to consumers, and then ignores the arguments for informing consumers in the case of irradiated food ingredients. The importance of giving consumers the right to choose is not obliterated by the combination of more than one food item into a food product, so food ingredients should be treated the same as individual food items. FDA did not reveal its selective interpretation of its own rules regarding the labeling of irradiated foods in its proposed rule, so the issue of food ingredients was not addressed in the comments on the proposed rules. Nothing in current law (21 CFR 179) nor in the FDA regulation states that irradiated ingredients are exempt from labeling. Under these regulations, many foods could therefore be exempted from the labeling requirement under the ingredients loophole * * *. Evidence to be presented at the hearings will include consumer demands to be properly informed about the processes to which food has been subjected, the ability of food processors to provide the required labels for food ingredients as well as for individual food items, the logic and necessity of extending the labeling requirements to food ingredients. Evidence would be presented by various consumer organizations such as the National Coalition to Stop Food Irradiation, Coalition for Alternatives in Nutrition and Healthcare, and market research experts, physicians, and scientists.

(HEI Para. III.)

Before establishing a labeling requirement, the agency must have some evidence that such a requirement is necessary and consistent with the

law.[10] The act requires that the label of a food fabricated from two or more ingredients bear the common or usual name of each ingredient (except that spices, flavorings, and colorings need not be declared by name) (21 U.S.C. 343(i)). The act does not require that the label declare details of processing for each ingredient. Special labeling could be required if the processing is material in light of representations made for the food or material with respect to consequences that may result from using the food (21 U.S.C. 321(n)).

FDA concluded that finished foods that had been irradiated should bear special labeling because such processing could cause changes in organoleptic or storage properties. Such changes could be significant in light of the fact that such foods would be perceived as unprocessed without special labeling (51 FR 13376 at 13388, 13389). On the other hand, FDA had no evidence that irradiation of an ingredient would affect the characteristics of a multiple ingredient food in any significant way. Therefore, the agency concluded that the labeling requirements for irradiated ingredients should be the same as for any other processed ingredients, namely, to declare them by their common or usual name without any requirement for stating whether they were processed (51 FR 13376 at 13389).

To justify a hearing, the objectors must proffer evidence that raises an issue of fact with respect to the agency's finding. The objector would have to present evidence that irradiation of an ingredient affected the final product to such an extent that the common or usual name was no longer appropriate, or that the consequences that may result from use of the final food are such that the consumer needs advance notice that an ingredient has been irradiated. HEI has failed to proffer any such evidence, however. HEI merely has stated that it would present evidence from various consumer organizations at a hearing. A hearing cannot be justified on the basis of a promise that some unidentified evidence will be provided at the time of the hearing.

The contention that labeling for irradiated ingredients was not addressed in the proposal is not correct. In the February 14, 1984, proposal (49 FR 5714), FDA requested comment on: (1) Whether it should require any type of label statement on food that has been treated by irradiation; and (2) if so, whether the statement should be required only on every food that has been irradiated (first generation food) or also on finished food with respect to each irradiated ingredient (second generation food) (see 49 FR 5714 at 5718). In the proposal, the agency set out its tentative conclusion that special labeling need not be required either when an ingredient was irradiated, or when a whole food was irradiated, and it requested comment on that tentative conclusion. FDA ultimately changed its mind and concluded that all foods that have been irradiated should bear special labeling. However, the agency also concluded that it could find no reason to require special labeling of a food that contains an ingredient processed by irradiation. Thus, the agency did in fact give notice in the proposal that it would consider whether to require special labeling of foods that contain irradiated ingredients.

The objector's statement that neither the current law nor FDA regulations state that irradiated ingredients are exempt from labeling raises an issue of law. Thus, it cannot serve as a basis for a hearing because a hearing will be granted only on the basis of a substantial issue of fact, not on issues of policy or law (21 CFR 12.24(b)(1)). Moreover, the agency has not exempted irradiated ingredients from any requirement of law or regulation. It has simply required special labeling for a finished food that has been irradiated so that consumers will know that it has been processed. As stated earlier, the act requires only that the presence of an ingredient be declared on a label, not a declaration of whether the ingredient has been processed. The objectors have proffered no rationale for concluding that the labeling requirement in this rule is inconsistent with the law.

V. Source of Radiation

One objection to the irradiated pork rule, from a radiation processing company, stated that the sources of radiation should not be limited to cobalt-60 and cesium-137 but should be consistent with the text and the spirit of § 179.26 in the proposed omnibus regulation. The objector requested a hearing.

A hearing will not be granted on factual issues that are not determinative to modifying the regulation (21 CFR 12.24(b)(4)). The irradiated pork rule was based on a petition limited to the two sources of radiation listed. Thus, the objector in requesting consideration of the use of an electron beam source is raising an issue that was not part of that rulemaking. However, in the rulemaking resulting in the omnibus rule, the agency considered use of all radiation sources and issued a rule that permits the use of an electron beam source for the use sought by the objector. Therefore, this objection is moot and needs no further consideration.

VI. Worker Safety

FDA referred comments on the proposed omnibus rule that related to worker safety and plant safety to the Occupational Safety and Health Administration (OSHA) and the Nuclear Regulatory Commission (NRC) because those agencies have jurisdiction over such issues. They advised FDA that current regulatory procedures are adequate to ensure the safety of the worker and of the general public (51 FR 13376 at 13395). HEI requested a hearing, stating:

> The FDA has promulgated a regulation to allow food irradiation using radioactive sources, x-ray equipment, and electron beam equipment without requiring proper and adequate regulations regarding equipment, periodic inspection of facilities and equipment, training of personnel, and related necessary regulations to ensure both worker safety and the safety of the general public.

(HEI Para. IV)

A hearing will not be granted on questions related to regulatory authority outside of FDA's jurisdiction (21 CFR 12.24(b)(5)). The agency stated in the omnibus rule that regulations on worker safety and public safety are governed by laws administered by government agencies other than the FDA. If the objector has any evidence demonstrating that worker safety or the safety of the general public in the vicinity of radiation facilities is not being protected adequately, it should submit such evidence to the agency with regulatory control over operation of the facility. Instead, HEI asserts that FDA's regulation concerning the safety of food does not impose requirements that are properly considered by other agencies under other laws. HEI has proffered no legal basis for issuing worker safety requirements in a food additive regulation nor any reason why its concern is not the proper responsibility of other agencies. Nor has it proffered any factual evidence to support its allegation that current regulations are inadequate. Thus, HEI has not provided any basis for a hearing.

VII. Environmental Impact

In the March 27, 1981, advance notice of proposed rulemaking, the agency requested comments on all aspects of food irradiation, including any environmental impact (46 FR 18992 at

[10] With respect to food labeling, the consumer's right to know has been defined by Congress in the requirements of the Federal Food, Drug, and Cosmetic Act. The agency has no basis to impose additional requirements once a manufacturer has met the statutory obligation.

18993). The agency considered the potential environmental impact when preparing the 1984 proposal and stated that: (1) existing safeguards in the Occupational Safety and Health Administration (OSHA), the Nuclear Regulatory Commission (NRC), the Department of Transportation (DOT), and FDA regulations are adequate to ensure that there will be no adverse environmental impact; (2) radiolytic products formed during processing are of no environmental concern and to the extent that irradiation would replace fumigation by toxic chemicals, it would reduce the amount of toxic residues entering the environment from fumigation; and (3) no evidence exists that exposure to radiation will result in mutant pathogens (49 FR 5714 at 5721). The agency tentatively concluded that the action would not have a significant impact on the human environment and announced that its finding of no significant impact and its environmental assessment document were available for public review. The agency responded to comments on this issue in the omnibus rule and concluded that none of the comments provided any information that would cause it to alter its previous determination (51 FR 13376 at 13395 and 13396).

A. Inadequate Review

HEI requested a hearing on a claim that the regulation allowed greatly expanded uses of food irradiation without an adequate environmental assessment or an appropriate environmental impact statement. HEI's claim was based on two contentions: (1) that there is insufficient assurance that the government agencies responsible for protecting the public from radiation are capable of carrying out that responsibility, and (2) that FDA did not document its claim in the omnibus rule that concerns over the formation of mutant pathogens at food irradiation facilities are unfounded. With respect to the second contention, HEI stated:

> Evidence will be presented from the scientific literature and from appropriate scientists regarding the probability and danger of mutant pathogens being created, and the need for further environmental assessment and preparation of an environmental impact statement regarding this issue.

(HEI Para. V.)

Neither of HEI's contentions justifies a hearing. A hearing will not be granted on the basis of mere allegations or general descriptions of positions and contentions (21 CFR 12.24(b)(2)). HEI must, at a minimum, "raise a material issue concerning which a meaningful hearing might be held." *Pineapple Growers Ass'n of Hawaii* v. *FDA, supra.*

HEI's first contention merely states an opinion that laws on worker and public safety are not properly enforced. As discussed earlier, before it issued its omnibus rule, FDA was advised by the relevant agencies that current regulatory procedures are adequate to ensure that there will be no adverse environmental effects either to the worker or the general public. If HEI wishes to challenge current regulatory procedures, HEI should raise the issue with the agencies in question.

The second contention simply disagrees with FDA's conclusion on the likelihood of producing mutant microorganisms that are more virulant or harmful than the parent microorganism. The agency has responded to this issue earlier in the section on "Mutation of microorganisms." HEI has not proffered any evidence in support of this contention and, thus, has not justified a hearing.

B. Environmental Assessment

In the irradiated pork rule published on July 22, 1985, the agency stated that FDA's environmental regulations (21 CFR Part 25) had been replaced by a more recent rule published in the **Federal Register** of April 26, 1985 (50 FR 16636), and cited the new section that would be applicable to a decision of this type. The new environmental regulation, which became effective on July 25, 1985, set forth policies and supplemental procedures for compliance with the National Environmental Policy Act of 1969 (NEPA).

Several objections to the irradiated pork rule requested a hearing and stated that FDA issued its rule on July 22, 1985, to avoid doing an environmental assessment according to the environmental rules that became effective July 25, 1985.

The accusation that FDA ignored its environmental rule is without merit. The environmental rule that became effective on July 25, 1985, did not establish any requirements that were not followed by FDA in its July 22, 1985, decision. On December 11, 1979 (44 FR 71742), FDA stated in its proposal to revise its rules governing the preparation of environmental impact documents under NEPA, that it would follow the procedures required by that proposal pending publication of the final rule. The final environmental rule that became effective July 25, 1985, did not change those procedures. The objectors have not cited any aspect of the new environmental regulation that was not satisfied by the procedures that the agency followed in adopting the irradiated pork rule. Thus, the objectors have failed to demonstrate that an issue of fact exists and therefore have not justified a hearing under 21 CFR 12.24(b)(1).

C. Petitioner Cited for Violations

Several objections requested a hearing and stated that the petitioner for the irradiated pork rule was cited for safety and environmental violations and should not be entrusted with the safety of food.

A hearing will not be granted on factual issues that are not determinative to the action requested (21 CFR 12.24(b)(4)). A food additive regulation is not a license for an individual petitioner but is a conclusion that actions in compliance with the regulation are safe. The fact that a petitioner was cited for violations is not relevant to whether the use of irradiation to treat food under the conditions of the regulation is safe. Therefore, such information is not a basis for granting a hearing.

VIII. 30-Day Objection Period

Notice was given in the **Federal Register** of July 23, 1984 (50 FR 29682), that FDA was considering a petition to permit irradiation of pork. The irradiated pork regulation, issued a year later on July 22, 1985, provided for a 30-day period for anyone adversely affected by the ruling to file an objection.

Several objections to the irradiated pork rule requested a hearing and stated that the 30-day time period for filing objections is unrealistic and particularly unfair and discriminatory to those located away from the Washington, DC, area.

A hearing will not be granted on issues of policy or law (21 FR 12.24(b)(1)). The time period for objections is established by statute. Section 409(f) of the act (21 U.S.C. 348(f)) provides that any person adversely affected by publication of an order may file objections within 30 days after such order. Thus, the time period for objections is not an issue on which a hearing can be held.

IX. References

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X. Summary and Conclusions

Based on a comprehensive evaluation of all relevant evidence, the agency concluded that food irradiated under the conditions of the April 18, 1986, omnibus final rule and the July 22, 1985, irradiated pork final rule is safe. The agency received objections to these rules relating to food safety, nutritional quality, labeling, worker safety, environmental impact, the statutory objection period, and the permitted sources of radiation. The agency has determined that the information submitted by the objectors does not raise material issues of fact that would justify an evidentiary hearing on any of the objections. The agency has also determined that the objections do not demonstrate a basis for revoking or amending the regulations except for clarifying wording on the items permitted to be irradiated. Thus, for the reasons stated in the discussions above, FDA is responding to the objections by amending the regulation as stated below and by denying all requests for a hearing.

XI. Objections

Any person who will be adversely affected by the amendment to § 179.26(b) regarding the description of aromatic vegetable substances may at any time on or before January 30, 1988 file with the Dockets Management Branch (address above) written objections thereto. Each objection shall be separately numbered, and each numbered objection shall specify with particularity the provisions of the regulation to which objection is made and the grounds for the objection. Each numbered objection on which a hearing is requested shall specifically so state. Failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held. Failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Three copies of all documents shall be submitted and shall be identified with the docket number found in brackets in the heading of this document. Any objections received in response to the regulation may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 179

Food additives, Food labeling, Food packaging, Irradiation of foods, Radiation protection, Reporting and recordkeeping requirements, Signs and symbols.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, Part 179 is amended to read as follows:

PART 179—IRRADIATION IN THE PRODUCTION, PROCESSING, AND HANDLING OF FOOD

1. The authority citation for 21 CFR Part 179 continues to read as follows:

Authority: Secs. 201(s), 409, 72 Stat. 1784–1788 as amended (21 U.S.C. 321(s), 348); 21 CFR 5.10; §§ 179.25 and 179.26 also are issued under secs. 402, 403, 703, 704, 52 Stat. 1046–1048 as amended, 1057, 67 Stat. 477 as amended (21 U.S.C. 342, 343, 373, 374); 21 CFR 5.10, 5.11.

2. Section 179.26 is amended in the table in paragraph (b) by revising the fifth entry under the headings "Use" and "Limitations" to read as follows:

§ 179.26 Ionizing radiation for the treatment of food.

* * * * *

(b) * * *

Use	Limitations
* * * * *	
For microbial disinfection of the following dry or dehydrated aromatic vegetable substances when used as ingredients in small amounts solely for flavoring or aroma: culinary herbs, seeds, spices, vegetable seasonings that are used to impart flavor but that are not either represented as, or appear to be, a vegetable that is eaten for its own sake, and blends of these aromatic vegetable substances. Turmeric and paprika may also be irradiated when they are to be used as color additives.	Not to exceed 30 kGy (3 Mrad).
* * * * *	

* * * * *

Dated: December 21, 1988.

John M. Taylor,

Associate Commissioner for Regulatory Affairs.

[FR Doc. 88-29885 Filed 12-29-88; 8:45 am]

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